FOOD AND DRUG ADMINISTRATION

CENTER FOR TOBACCO PRODUCTS

TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE

(TPSAC)

THURSDAY, MARCH 17, 2011

1:00 p.m. to 5:00 p.m.

FDA White Oak Campus

White Oak Conference Center

Building 31, The Great Room

Silver Spring, Maryland

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C O N T E N T S

P R O C E E D I N G S

(1:23 p.m.)

Call to Order

DR. SAMET: Good afternoon. We'll go ahead and get started with the meeting of the Tobacco Products Scientific Advisory Committee. Sorry to be a little bit late. I'm Jon Samet, the chair of the committee. I want to thank you all for joining us. I need to make a few statements, and then we will introduce the committee.

For topics such as those being discussed at today's meeting, there are often a variety of opinions, some of which are quite strongly held. Our goal is that today's meeting will be a fair and open forum for discussion of these issues and that individuals can express their views without interruption. Thus, as a general reminder, individuals will be allowed to speak into the record only if recognized by the chair. We look forward to a productive meeting.

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine

Act, we ask that the advisory committee members take care that their conversations about the topics at hand take place in the open forum of the meeting.

We are aware that members of the media are anxious to speak with the FDA about these proceedings. However, FDA will refrain from discussing the details of this meeting with the media until its conclusion. Also, the committee is reminded to please refrain from discussing the meeting topics during breaks. Thank you.

Now, let's see. Let me ask the committee to make introductions. I think, actually -- on the phone -- I failed. Caryn's going to read the statement, and then we're going to introduce the committee. How could I mess up so badly after this training?

Conflict of Interest Statement

MS. COHEN: The Food and Drug Administration is convening today's meeting of the Tobacco Products Scientific Advisory Committee under the authority of the Federal Advisory Committee Act.

With the exception of the industry representatives, all members and non-voting members are special government employees or regular federal employees from other agencies and are subject to federal conflict of interest laws and regulations.

The following information on the status of this committee's compliance with federal ethics and conflict of interest laws, covered by but not limited to those found at 18 U.S.C., Section 208 and Section 712 of the Food, Drug, and Cosmetic Act, is being provided to participants in today's meeting and to the public.

FDA has determined that members of this committee are in compliance with the federal ethics and conflict of interest laws. Under 18 U.S.C., Section 208, Congress has authorized FDA to grant waivers to special government employees and regular federal employees who have potential financial conflicts when it is determined that the agency's need for a particular individual's services outweighs his or her potential financial conflict of interest.

Under Section 712 of the FD&C Act, Congress has authorized FDA to grant waivers to special government employees and regular federal employees with potential financial conflicts, when necessary, to afford the committee essential expertise.

Related to the discussion of today's meeting, members of this committee have been screened for potential financial conflicts of interests of their own, as well as those imputed to them, including those of their spouses or minor children, and, for purposes of 18 U.S.C. Section 208, their employers. These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties, and primary employment.

Today's agenda involves receiving an update on the Menthol Report Subcommittee; receiving and discussing presentations regarding the data requested by the committee at the March 30th-31st, 2010 meeting of the Tobacco Products Scientific Advisory Committee.

This is a particular matters meeting, during which general issues will be discussed. Based on the agenda for today's meeting and all financial interests reported by the committee members, no conflict of interest waivers have been issued in connection with this meeting.

To ensure transparency, we encourage all committee members to disclose any public statements that they have made concerning the issues before the committee. With respect to FDA's invited industry representatives, we would like to disclose that Drs. Daniel Heck and John Lauterbach and Mr. Arnold Hamm are participating in this meeting as non-voting industry representatives, acting on the behalf of the interests of the tobacco manufacturing industry, the small business tobacco manufacturing industry, and tobacco growers, respectively. Their role at this meeting is to represent these industries in general and not any particular company.

Dr. Heck is employed by Lorillard Tobacco Company, Dr. Lauterbach is employed by Lauterbach &

Associates, LLC, and Mr. Hamm is retired. FDA encourages all other participants to advise the committee of any financial relationships they may have with any firms at issue.

I'd like to ask you all to please silence your cell phones if you have not already done so. And I'd like to introduce our press contacts, Dr. Tesfa Alexander and Jeffrey Ventura. If you're here, please stand up. Thank you.

Introduction of Committee Members

DR. SAMET: Now is my chance?

Now, we'll do the committee introductions.

Arnold, why don't we start with you?

MR. HAMM: Arnold Hamm, tobacco grower representative.

DR. LAUTERBACH: John Lauterbach, Lauterbach and Associates, representing small business tobacco manufacturers.

DR. HECK: Dan Heck of Lorillard Tobacco Company, representing the tobacco industry.

DR. MCAFEE: Tim McAfee, representing the Center for Disease Control.

DR. HATSUKAMI: Dorothy Hatsukami from the University of Minnesota.

DR. CLANTON: Mark Clanton representing pediatrics, public health, and oncology.

DR. HENDERSON: Patricia Nez Henderson, Black Hills Center for American Indian Health.

MS. DELEEUW: Karen DeLeeuw, representing state government.

DR. HUSTEN: Corinne Husten, Center for Tobacco Products

DR. ASHLEY: David Ashley, Center for Tobacco Products.

DR. SAMET: Then on the phone, Melanie?

DR. WAKEFIELD: Yes. It's Melanie Wakefield from The Cancer Council Victoria in Melbourne, Australia.

DR. SAMET: Neal?

DR. BENOWITZ: Neal Benowitz, University of California San Francisco.

DR. SAMET: Do we have any of our other ex-officio members on the phone?

[No response.]

DR. SAMET: Okay. And Jack Henningfield will be here shortly.

So let's see. Corinne, let me turn to you.

FDA Presentation: The Menthol Report

DR. HUSTEN: As you know, the charge to the committee is to produce a report and recommendations on the impact of menthol cigarettes on public health, including such use among children, African Americans, Hispanics, and other racial and ethnic minorities. The report is due March 23rd of this year.

So what to expect from this point on. The menthol report and recommendations will be deliberated on and finalized at the conclusion of this meeting. The report will be made available to the public on FDA's website once it's been reviewed for redaction of any trade secret or commercial confidential information. The industry perspective document will also be reviewed by FDA as part of its review of the science on menthol, and it will be posted on the website as well.

Once the report is received, FDA will

consider the report and recommendations of the committee, the industry perspective document, and other relevant scientific information concerning menthol cigarettes and make a determination about what actions, if any, are warranted. There's no required deadline or timeline for FDA to make such a determination. Any sales, distribution restrictions, or product standards would be implemented through notice and comment rulemaking.

So this is today's meeting, but it's actually today's and tomorrow's meeting. So the topic of the meeting over these two days is presentation of the final model of the impact of menthol on initiation and cessation, an open public hearing discussion of the remaining TPSAC report chapters, discussion of the TPSAC conclusions, and discussion of the TPSAC recommendations.

As you recall from an earlier meeting, the committee had outlined a set of questions that they were proposing to answer in this report. Some of these were related to individual smokers and some of them were related to the population. So the

questions related to individual smokers were, what's the level of evidence that the availability of menthol cigarettes increases the likelihood of experimentation?

What's the level of evidence that the availability of menthol cigarettes increases the likelihood of becoming a regular smoker?

What's the level of evidence that inclusion of menthol in cigarettes increases the likelihood of the smoker becoming addicted?

What's the level of evidence that the inclusion of menthol in cigarettes increases the degree of addiction of the smoker?

What's the level of evidence that smokers of menthol cigarettes are less likely to quit successfully than smokers of non-menthol cigarettes?

What's the level of evidence from biomarker studies that smokers of menthol cigarettes receive greater doses of harmful agents per cigarettes smoked in comparison with smokers of non-menthol cigarettes?

What's the level of evidence that smokers of menthol cigarettes have increased risk of disease caused by smoking, in comparison with smokers of non-menthol cigarettes?

The questions related to smoking at the population level were, what's the level of evidence that the availability of menthol cigarettes increases the prevalence of smoking in the population beyond the anticipated prevalence if such cigarettes were not available? And also to consider within subgroups within the population.

What's the level of evidence that tobacco company marketing of menthol cigarettes increases the prevalence of smoking beyond the anticipated prevalence of such cigarettes if such cigarettes were not available? And again, with consideration of subgroups within the population.

The other questions for the committee over the course of the meeting are what are the overall conclusions of the menthol report? What are the conclusions of the committee regarding the public health impact of the use of menthol in cigarettes?

What are the recommendations of the committee regarding the use of menthol in cigarettes? And those are the questions before the committee at this meeting.

Any clarifying questions?

DR. SAMET: Any questions for Corinne?

[No response.]

DR. SAMET: Okay. Thank you.

Our next item on the agenda for today is to hear again from David Mendez from the University of Michigan. This will be yet another presentation from David concerning the population dynamics model that he has developed to assess the consequences of menthol cigarettes.

David, thank you once more.

Presentation – David Mendez

DR. MENDEZ: Thank you and good afternoon. Again, I'm David Mendez from the University of Michigan. I've come here to present the results of the population dynamic model to evaluate the consequences of menthol cigarettes on the population.

This work was done under a contract with the Center for Tobacco Products, but the content and conclusions of this presentation and the report that I'm going to produce are just my own.

So the general model, as we discussed before, is a compartmental model. And we followed a population of smokers, the whole population of the United States, from age zero to age 100 and from the years 2010 to 2050. And we separate the population into never-smokers, current smokers of menthol and non-menthol, and former smokers.

So the model just shows the flow diagram of the transition from one category to another category. And the boxes represent the accumulation of individuals in those categories. And the specific subdivisions within those boxes are age smoking status, and specifically for the former smokers, we just don't keep track -- the model doesn't just keep track of age and year, but it also keeps track of years since quit. So we can see that we can actually evaluate the diminishing relative risk of former smokers.

The parameters that control the model are the circles, and they are separated into two different types of circles. The green circles represent the parameters that we had from the general population or they're publicly available to evaluate a model like this with no menthol in mind. And the red parameters, the red circles, represent the parameters that are specifically related to menthol, and that will drive the model.

So those parameters that are in circles, I'm going to talk a little bit about that now. They were supplied by TPSAC after a careful literature review. And they also provided some estimates of ranges for the general population about the minimum and maximum of those parameters.

The parameters are the proportion of menthol among initiators, for example. So that's the first one, is what proportion of people who initiate smoking are menthol versus non-menthol? And it was for the general population set to 40 percent. The proportion of menthol among experimenters; so from the individuals that are experimenting to start

smoking -- before they started smoking, what is the proportion of them that experiment with menthol, and it was set to 45 percent.

Then the next parameter is the ratio of the yields from experimenter to regular smokers. So what is the difference or relative likelihood of becoming a smoker if one experiments with menthol versus non-menthol? And it was set, because of looking at parameters in the literature, at 1.68, meaning that a person who experiments -- in this case, a person who would experiment with menthol cigarettes is 68 percent more likely to become an initiator, either menthol or non-menthol, than a person who experiments with a non-menthol cigarette.

The cessation rates ratio, menthol to non-menthol, we set at .95. That's a TPSAC estimate; that is that menthol cigarettes are a little bit more -- have a little bit slower quitting rate than the non-menthol cigarette. The mortality risk ratio, menthol to non-menthol, was set up at 1 as the most likely TPSAC estimate. So there's no

difference in mortality. And switching rate from menthol to non-menthol and from non-menthol to menthol was taken from the Switching Book, and those are the parameters, 1.8 percent and .8 percent.

So in order to figure it out, in order to compute, what is the burden of menthol -- what is the impact of menthol on the population with those parameters, then we set up scenarios that, first, they take the TPSAC estimate and compare that development of the model from year 2010 to year 2050 with a counterfactual within this scenario, with an alternative scenario, where there is no menthol.

So it's important to distinguish that this experiment doesn't model a ban. What it's modeling is a world, supposed world in 2010 where there is no menthol at all. And the initial prevalence of that world without menthol, we set up at the same exact prevalence as the actual prevalence in 2010. So they have the same point.

Now, for the counterfactual scenario, the

initiation rate, we used the same cessation rates as the non-menthol smokers in that, that was derived from the model. And the initiation rate was set at 16.7 percent instead of 21.8 percent, but that's derived from the estimates, derived from the parameters, as we will see in the next slide, how this 6.7 [sic] percent comes directly from the parameters that were supplied by TPSAC.

Again, the counterfactuals assume that menthol does not exist and the initial prevalence is the same between the counterfactual and the scenario, the TPSAC scenario. And the excess figures that we are going to present, when it says excess, the figures represent the difference of the scenarios, minus a constant, or the scenarios minus the counterfactual.

So what I do with the model is take a look at what would happen under current circumstances from 2010 to 2050, and measure the cumulative number of deaths under that scenario, and then going to the counterfactual, and measure also the number of deaths, and then report the difference

between the two.

So a point of clarification, how the initiation rate under counterfactual came about, conceptually, this is the issue. So we have a group of experimenters, and that group of experimenters becomes initiators. And then there's a yield; some group of experimenters experiment with menthol and some groups experiment with non-menthol. So we know that there's a difference in yield between the menthol and non-menthol, and that ratio is available in the literature.

So if we under the counterfactual assume now that menthol doesn't exist, the yield of the non-menthol will produce initiation under the same proportion of experimenters without changing the proportion of experimenters. We're not assuming that they're going to be less or more experimenters, the same, but there's going to be a yield, a lower yield, with those parameters. And that's how we get our counterfactual numbers.

So these are the results of the general population model, and those boxes keep track of the

counterfactual, and the TPSAC scenario, and balance what happens in one scenario versus the other in each one of the categories. The interesting -- and actually the total figure are shown and highlighted in green. So we end up, according to the model, with an excess cumulative death of about 327,000 excess deaths attributed to menthol, with the comparison between the menthol and non-menthol world, and about 9-some million excess initiators between the two.

Let me get back here. All this minimum and maximum parameters were tested one by one to figure out what is the sensitivity of the model to those parameters. And both the excess death and the excess initiation are shown. So if you take a look at 2050 and the column of 2650 [sic], it gives you the difference in excess death when we put all these parameter ranges. I just put this here in a graph so we can see it in perspective there.

The leftmost column represents the cumulative excess death under the TPSAC scenario. This is the most likely or the best estimates. And

the rest represents what happened under sensitivity of the parameters. So, for example, one extreme sensitivity, the first very low, that parameter or excess death that you see is the low yield from experimenter to a smoker.

So if we assume, for example -- in this case, the minimum range was set up to 1. If we assume that there is no difference between a menthol and non-menthol in producing, in going from experimenting to smoker, regular established smoker, then the difference in the model will be on cessation because the initiation will be the same. And that cessation will produce about 30,000-something excess deaths, because the difference in cessation was set very low, set at about 95 percent of the non-menthol smokers.

Another low and high that you see, if we take a look at the big ranges on the mortality risk that we have, low menthol mortality risk is set at .8., and it ends up being menthol, slightly protective, and high menthol mortality risk ends up with -- which is set up to 1.2, end up to be over

600,000 deaths by 2050.

So these are the results for the general population, and most of the parameters are pretty consistent.

The African-American population, we have the TPSAC estimates on the left. And for some of the parameters, we didn't have a good specific range to do a lot of sensitivity analysis. And for the parameters that we have sensitivity ranges, it didn't -- the model was not very sensitive to that. So instead of doing a full-blown sensitivity analysis, which pretty much is going to show the same pattern, what I did is compare the most likely values for the African-American population with a hypothetical low menthol prevalence in the African-American population.

So this hypothetical population is exactly the same as the African-American population, the same age structure, the same prevalence, exactly the same age distribution, the same mortality, and excess, and relative risk, except that that population will have the same menthol prevalence as

the general population.

So the idea is, analyze that population and see what is the difference between the two; what is the extra burden that is causing the African-American population -- because of their high menthol population. Okay?

So first I'm going to show the results for the African-American population. By the way, the African-American model was set up with parameters that are totally appropriate for African Americans. The death rates were set up as the specific background death rates for African Americans, and the relative risks for smoking were set up as the appropriate relative risks for African-American smokers. I obtained them from the American Cancer Society. They run analyses with CPS-2 data and they provided that to me. So they are specific parameters for the African-American population.

Now, the proportion of menthol initiators and the proportion of menthol experimenters, that is set up at .8. So the proportion of people within the African-American population that

experiments with menthol is 80 percent. The proportion of initiators that smoke menthol in the African-American population is 80 percent. And then the rest of the parameters are pretty much the same yield ratio as we use in the general population; the .95, the same difference in cessation that we use in the general population, the same mortality risk, 1, so they are implying that there's no mortality difference. And the switching they are taking from the Switching Book and they are appropriate for the African-American population.

The initiation rate, applying those parameters now, applying the parameter of the proportion of menthol among experimenters and looking back at the procedure that I show here, will yield a lower initiation rate under this scenario. So instead of the 19.8 percent of -- that prevalence at age 20, the most recent data that I got for prevalence, age 20 (unclear) is specific for African Americans, so that went down to 12.7 percent. And then we'll talk a little bit

later about the hypothetical of menthol prevalence population.

So these are the set-up for the African-American population under the best estimate of TPSAC, and when we run the model, these are the solutions -- the results. We end up -- sorry; this is difficult to see -- at about 66,000 extra deaths in 2050 and 1.6 million extra initiators by 2050.

So now, if we analyze the hypothetical low African-American population, the first two parameters will be the proportion of menthol among initiators and proportion of menthol among experimenters, .4 and .45, which is the same as the general population. And then the rest of the parameters are the parameters for the African-American population, and the initiation rate -- because the proportion of menthol experimenters change, then the counterfactual initiation rate changes, and that will give us the -- that will give us the idea of the extra burden in that specific population.

So when we run that scenario, we end up with

44,000 deaths by 2050. So if you compare the two scenarios, by 2050, in the African-American population, we would have an excess death, a cumulative excess death of about 67,000. But if the African-American population didn't have the high menthol proportion -- or if the African-American population had the menthol proportion of the general population, we would end up doing this analysis with 44,000 excess deaths.

So the difference is the extra burden caused in the African-American population because it's specifically menthol. And the difference between the two excess initiation, 1.6 million versus 1.1 million cumulative by the year 2050.

So all these analyses, we have submitted in a report to the Center for Tobacco Products. Every single detail of the model, all the derivations, calculations, and structures of the model are described in detail in that report. And all the data that I used in order to produce this estimate or these results are all publicly available. So I will entertain any questions now.

DR. SAMET: Thank you. I think we have plenty of time for discussing this update on your report. I think it might be useful -- I just want to check and make sure my understanding of the counterfactuals is correct. I think this goes back -- David, if you could go to your -- I think it's the fourth or fifth slide. Actually, the next one.

So if I understand -- and just make sure I have this correct -- in the counterfactual scenario, the prevalence of smoking is the same in the actual or business as usual in counterfactual scenarios; the initiation rate is lower at age 18.

DR. MENDEZ: Yes. So the initial prevalence is the same. We start with the same prevalence in two populations. The initiation rate, which is the initiation rate that I'm going to use in the counterfactual, is lower, indicating the fact that now we have the non-menthol experimenters that are the ones that are going to be produced -- that are going to become regular smokers and that they have a lower yield. And the lower yield is computed in

this fashion.

DR. SAMET: So if you go forward to the input parameters for the African-American model -- and I guess I want to make sure I understand this. So here you now have the high menthol TPSAC estimates.

DR. MENDEZ: Yes.

DR. SAMET: And then the initiation rate goes up under the counterfactual, as shown here. So let me just make sure I understand that, because now the proportion of menthol is halved.

DR. MENDEZ: Well, if you have more menthol, if you take that menthol out, the initiation rate is lower. I mean, if this menthol is more important to you and you take menthol out, your initiation rate --

DR. SAMET: Right. So that's why under the -- in the TPSAC estimates, you have 12.7, and then in the hypothetical low menthol prevalence, it's 15.

DR. MENDEZ: Yes. Because the menthol is less important in that population, so we start with

those populations here.

DR. SAMET: Okay. I think I have that.

Dan?

DR. HECK: Yes. Dr. Mendez, upon your slide 4 -- if we can just go back to the general population, I think some of the same questions I have might apply to some of the later slides as well. It appears to me, from my understanding, that this ratio, the K5, 1.68 here -- and I think it may have been 1.61 in an earlier presentation -- but that seems to be the key number that's really driving the output from this model.

So I think if this committee's going to embrace the model as useful in the end, we really have to have some high confidence that that number is a real representation.

Where did that number come from? Can you refresh my memory? I think that Neal Benowitz may have asked this question in a prior meeting. I don't recall the answer. The K5 value here, 1.68, what was the source of that?

DR. SAMET: Dorothy, do you want to speak to

that question?

DR. HATSUKAMI: So the source for that was a Nonnemaker article. We used that as a source primarily because there have been no other studies that have been done, looking at the likelihood of experimenters becoming established smokers.

DR. HECK: So this key value then was derived from a single paper that, as I recall, was I think provided to us in January or November, an unpublished paper. And as my recollection is, the youth population survey there was around just over 100. And the number of black youth was around a dozen.

To me, that just seems like a fairly frail basis to have found the whole driver of this model output on. I realize there's a shortage of useful data in this area, and I think that's one of the problems we all face. I'm recalling, too from the Nonnemaker study that that 1.68 ratio was not statistically significantly different from – or, that is the transition of menthol smokers from experimentation to initiation was not significantly

different than that of non-menthol smokers.

So again, it just brings me back to this key value and this model being based on a relatively small single unpublished study that did not show statistical significance. And I just would suggest or present to the committee my concern that that's a frail basis to employ in making such projections and calculations.

DR. HATSUKAMI: So Dan, I think the numbers that you refer to are really based upon the sample size that didn't include wave 3. As you recall, there had been wave 1, wave 2, wave 3. And what we decided to do is pull on the numbers that did include wave 3 in large part because we thought it would be important to increase the sample numbers. It is my recollection, in fact, that the 1.68 was significant.

DR. MENDEZ: Yes. It's my recollection, too, that that number is statistically significant.

DR. SAMET: Actually, just as a comment, I think if you look at the range of parameters, the minimum is 1 and you can see what happens if that

number is set equal to 1. And again, this is why we have included these ranges, so that sensitivity can be assessed. And obviously, if you compare the proper scenarios here, you can identify at least the ranges of what values would be for points between 1 and 1.68.

I agree it's always nice to have more data than one has, but you have to go with what you do have. And I think here what we have explored and what David has explored is the sensitivity of findings, to what you have correctly identified as one of the key model parameters.

DR. HECK: Yes. Just a small follow-up, Mr. Chairman. I'm going to have to go back and look at that paper again. There have been a lot of considerations here lately, but just maybe a general question. Does this model allow us to include an expression of the uncertainty, or confidence limits, or whatever about the output parameters?

DR. SAMET: David, do you want to comment?

DR. MENDEZ: I'm sorry. I didn't --

DR. SAMET: The question was, have you included some -- or how could one include some sort of probabilistic estimate of uncertainty, I think is what Dan's referring to.

DR. MENDEZ: Actually, part of the sensitivity analysis is putting that -- a model like this is very easy to just run into Monte Carlo mode, and it's set at range for the parameters and actually figure out what the dispersion is going to be in the output. So I don't know what specifically you -- but, yes. The model can do that.

DR. HECK: I just have some level of concern because it's 1.68 with two decimal places to the right of the decimal point. It kind of communicates a high degree of precision about this, so since this one factor seems to drive largely the output of this model, I just wanted to try to get a sense of how confident we are in terms of statistical confidence limits or whatever, with whatever estimates may be produced by the model.

DR. SAMET: I think it might be useful,

since we're nearing the end of this process, to say very clearly why these models have been done and what they'll be used for. And I think we are quite aware that numerical precision here is illusory and that that's not the goal of the modeling. It is to get a general understanding of what the approximate range of public health impact might be to address that component of our charge, the qualitative determinations of public health impact. And this is a way to gauge in I would say a roughly quantitative fashion what the numerical magnitude of that impact might be.

I tell you, we've seen one other relevant modeling exercise presented by David Levy I believe at our last meeting. And again, I see these tools and I think the writing group sees it similarly, that these are useful aids to try and understand what burden might be posed to public health by the availability of menthol cigarettes.

I can certainly agree with you that perhaps, when we say that the total cumulative excess deaths is 327,565, no one is going to stand firm and argue

for that particular number versus any other number. I think the point actually is what is the magnitude, and as you point out, that magnitude may be particularly sensitive to one or more of the modeling parameters or other details of model specification.

Let's see, other questions or clarifications for David? I think this is an important opportunity to review this, and I think the approach to the African-American population we've not seen before. So again I would encourage discussion of that.

Let me turn to Melanie and Neal, not to forget you. Any questions?

DR. BENOWITZ: None from me.

DR. SAMET: Melanie?

DR. WAKEFIELD: I don't have any, Jon. I thought it was a helpful presentation.

DR. SAMET: Oka. Mark?

DR. MENDEZ: Thank you.

DR. CLANTON: So you did the analysis using 10-year intervals, and I think I know the answer to

my own question. The output's probably proportional. But given that, the lead time to most chronic diseases that result from smoking, which include chronic obstructive lung disease, cancer, generally around 20 years, I'm just wondering if we used a 20-year interval, would it just be proportional to the time or would there be fundamental changes to the magnitude reported out in those cells?

DR. MENDEZ: The model doesn't do 10-year increments. It does year increments. I'm just reporting, yes, one year. So I'm reporting everything here as far as simplicity, but this actually follows every year.

DR. SAMET: Jack, welcome.

Any other questions? Because I'll ask a few more, if not.

[No response.]

DR. SAMET: So, David, I think just again probably for the sake of clarity about interpretation of the results, it is the difference between the, quote, "TPSAC estimates" and the low menthol

prevalence estimates, the difference that tells us about the consequences of having a prevalence of .8 of menthol cigarette use among smokers versus .4 –

DR. MENDEZ: Exactly.

DR. SAMET: -- and it's that difference that tells us the consequence of having a population with high menthol prevalence, menthol cigarette use.

DR. MENDEZ: With high menthol smoking --

DR. SAMET: So I just want to make sure that everyone understands that you would take 66,524, and maybe even round that off to something else, and subtract from that, the 44,771, and similarly, for the number of smokers, of excess smokers accumulated over time.

Then again, just to make sure everybody understands, the mortality estimates underlying this were obtained from CPS-2, from the American Cancer Society's CPS-2 study for African Americans within the cohort. And those estimates differ, in general, lower --

DR. MENDEZ: Lower than the general

population, yes.

DR. SAMET: -- than the general population estimates. I just want everybody to recognize that. Those aspects of the model have been tailored specifically to the African-American population, but as you can look at the assumptions on other parameters in the model, except for the prevalence, they're by and large the "TPSAC estimates."

So again, I just want to make sure everybody understands what has been presented.

Any other questions about this work? Thank you. You must be almost done.

[No response.]

DR. SAMET: Thank you. You just be almost done.

Okay. Thank you very much, David, for a lot of hard work in a very short time. We appreciate it.

DR. MENDEZ: Thank you.

Discussion of Menthol Report Chapters

DR. SAMET: So in the next segment, up to

break, we can turn back I think and discuss where the chapters stand and give an update, updated versions of -- let's see if I have this right – a version of chapters 1 and 2 have been previously posted and discussed. Chapter 3, I believe a slightly updated version, has been posted. Chapter 4, a draft has previously been seen and what we believe is approximately the final draft has now been posted. A draft of chapter 5, which is on marketing, is available at this time I think; yes, chapter 5, and posted. Chapter 6, which refers to initiation, becoming a regular smoker and cessation, is in progress and will be posted. Chapter 7 also will be posted. Sorry. Updated versions of chapters 7, which was discussed at the last meeting, and 3, will be posted.

If I have confused anybody with the chapter numbers, I apologize. But what we did was, chapter 5, which had been two chapters, was turned into two separate chapters because of their length.

So chapter 8 is the chapter that will provide the final conclusions and recommendations

to FDA. So shortly, all the chapters will be available except for chapter 6, which should be available rather soon, and then chapter 8, just to update.

So I think what we'll do is spend some time, then, I think -- I don't think there's a need to return to chapters 1, 2, or 3, just perhaps a quick update from Patricia and Karen about chapter 4 and any final changes made since our last discussion. So I'm not sure who wants to take the lead in this.

Patricia, thanks.

DR. HENDERSON: Yes. Chapter 4 is basically the chapter that provides the background to the work that we're doing, and it describes in detail the history of menthol, as well as the history of menthol marketing. And both Karen and I worked quite heavily on this.

Karen, do you want to add anything to some of the new input that we put into the chapter?

MS. DELEEUW: I don't think I have anything new, but certainly trying to figure out the scope of this chapter was the difficult part in terms of

where to draw the line around the history.

DR. SAMET: Again, as careful readers of the report, we'll note that some material may extend from -- the same material may be covered in one level or another in several different chapters, but that was done deliberately because we felt that such redundancy was appropriate.

Maybe, Melanie, perhaps you could just talk about chapter 5, again, which at our last meeting I think you gave quite a detailed summary of, and now that is available. But let me turn to you for comments on that updated chapter.

DR. WAKEFIELD: Sure. Thanks, Jon. Before I begin, I'd just like to acknowledge Dr. Lisa Henriksen, who's been very much involved in contributing to the writing of this chapter as a special government employee of FDA. At the last meeting, I indicated that we had made some decisions about some of the scope of this chapter. Some of the pieces had been allocated to different chapters.

So the questions that we have now framed the

chapter around flow much better I think. And overall there are six questions, and I can go through and give a bit of a summary of perhaps the answers to those questions if you would like, Jon.

DR. SAMET: I think we have some time for you to do that, so go ahead.

DR. WAKEFIELD: So the first question that we posed was with the menthol marketing, was different from -- or similar to non-menthol marketing in terms of product, place, price, promotion, and packaging. And overall, in looking at the evidence from a wide range of sources, we found that menthol cigarettes are marketed in fairly similar ways to non-menthol cigarettes in that the same sort of general marketing principles are employed.

We did find that there were some differences in relation to some types of promotional efforts. But in general these were relatively small and unsystematic. One difference that we were concerned about was that there was some evidence from some sources that price promotions might be

increasingly being used for menthol than non-menthol cigarettes, which could serve to reduce the price of menthol more than they reduce the price of non-menthol cigarettes. And we also noted that more menthol smokers than non-menthol smokers take advantage of price promotions, and this was especially the case for African Americans. But I guess not all the data sources that we examined did suggest this.

Much of the evidence that we reviewed on price was highly aggregated, and so the aggregated level of the data couldn't shed light on the use of menthol price promotions by different brands or by different tobacco companies, or the use of price promotions to target particular race and ethnic groups. And the aggregated data couldn't help us to examine the differential use of menthol price promotions around focal periods such as tobacco tax increases and other tobacco control policies.

So overall, we found the evidence to be insufficient, I guess, to conclude that retail marketing practices might be responsible for recent

increases in the proportion of smokers who smoke menthol cigarettes. And this is an area where we think that more research is needed to examine the relationship between the move to retail-based marketing, especially price promotions, and the increase in the proportion of smokers who smoke menthol cigarettes that we've observed recently.

The second question we looked at was what health reassurance messages were or are used in menthol marketing messages. And on the basis of tobacco industry document reviews and empirical studies, we found the evidence to be sufficient to conclude that menthol cigarettes have been and continue to be marketed with a set of associated branding elements and labels that connote health benefits.

These marketing messages originally included claims of explicit benefits of a medicinal nature, such as soothing of sore throat or clearing a blocked nose. But they've moved over time towards more implied health benefits through the use of powerful images of coolness and refreshment, the

use of the color green, which is associated with nature and healthiness, and the use of phrases and labels emphasizing the sensory experience of menthol cigarettes, such as terms like “refreshing and smooth.”

The third question that we thought to answer in this chapter was what kind of other messages were or are conveyed to consumers or potential consumers by menthol marketing. And we found that there were two other key kind of themes that were communicated in marketing messages. The first featured kind of a very youthful image and themes appealing to youthful audiences, themes of fun and silliness, group membership, peer acceptance, and so forth.

The second type of other message was I guess a theme of what we’ve called kind of in-group identity, sort of messages that appeal to -- although they’re designed around socially and culturally relevant messages, which appeal to different market segments. And we noted that the different in-group identities are emphasized in

marketing for different kinds of brand families.

So there's no single brand image that signifies necessarily a menthol smoker, although there is some suggestion that people do perceive menthol smokers to be a bit younger.

Who are the target populations for menthol marketing, and is there evidence to show that particular groups of the population were targeted, was the fourth question. In addressing this question, we reflected on the fact that it's basic marketing practice to identify primary market or primary target groups for marketing. And there's abundant evidence that this occurs in overall tobacco marketing, so it's no surprise that it also occurs in menthol marketing.

We found that there was sufficient evidence to conclude that menthol cigarettes are disproportionately marketed to younger smokers. We noted that there's evidence from tobacco industry documents, from the reviews that have been done, that the tobacco industry has designed menthol cigarettes with lower menthol yields. And there

has been an awareness in the tobacco industry that at lower menthol levels, the sensory effects of menthol reduce the harshness of cigarettes for new smokers.

In addition to messages that have implied health reassurance, menthol cigarette marketing has also promoted a very useful brand image than for non-menthol cigarettes, and it's particularly emphasized the role of menthol cigarettes in peer group acceptance. And as we know from chapter 4, menthol smoking is higher among youth and young adults compared with older adults.

We also looked particularly at African Americans as a target group, and there we found evidence to conclude that menthol cigarettes are disproportionately marketed to African Americans. They have been the subjects of specifically tailored menthol marketing strategies and messages.

There are empirical studies of billboard advertising and point-of-sale advertising for menthol cigarettes to show that those messages have been overrepresented in neighborhoods with a higher

percentage of African Americans and in magazines with a high African-American readership, also than non-menthol cigarette advertising. And consistent with these targeted marketing efforts, menthol cigarettes are disproportionately smoked by a high proportion of African-American smokers.

We also looked at Hispanics or Latinos as a subgroup, and we did find evidence to conclude that it's at least as likely as not that menthol cigarettes have also been disproportionately marketed to Hispanics as well. We see from chapter 4 that menthol smoking is higher in Hispanics than non-Hispanic whites.

Then the final set of groups that we looked at were females, and we also looked at Asian-Americans, and Hawaiians, and Pacific Islanders. And we did see that there had been certainly some tailoring of marketing to these groups, but we found insufficient evidence to conclude that they had been proportionately more targeted by menthol than non-menthol marketing and advertising.

Question number 5 asked whether menthol

marketing influences the perceived taste or sensory experience of menthol cigarettes. And in this area we did find evidence to conclude that menthol branding and messaging influences the perceived sensory experience of menthol cigarettes, and it contributes to the consumer's overall subjective evaluation and liking of the cigarettes.

So the last question was whether consumers perceived menthol cigarettes as safer or less harmful than non-menthol cigarettes, and here we also found evidence to conclude that consumers do hold beliefs about the medicinal benefits of menthol cigarettes and beliefs about other implicit health benefits. And this is especially the case among African Americans. And it does follow from some of the marketing claims that are made or the marketing messages. But we did note that in the context of widespread public education about the health harms of tobacco use, it's uncommon for consumers to state an explicit belief that menthol cigarettes are safer or less harmful than non-menthol cigarettes.

So that brings us to the end of our questions. And we certainly reviewed a lot of evidence to get to those conclusions, and I think the chapter runs to quite a few pages.

DR. SAMET: Okay. Thank you for a very thorough review of these topics. Now, I'll just mention that the sub-questions, for example, that are placed at the beginning of chapter 5 were particular to that chapter and that topic. And then we intend on answering the questions that you saw at the outset, presented by Corinne. We will combine evidence from the cross-chapters to answer those seven questions at the individual smoker level and the two questions at the population level.

So let me open up this chapter for discussion. Dan?

DR. HECK: Yes. There's a lot of material here, 40 plus pages seen for the first time here as I sit down. But I guess the last point you mentioned is freshest in my mind, the draft conclusion that menthol cigarette consumers

perceive those products to be less harmful, particularly for African Americans it says here, I'll be interested to see as I read into this how that conclusion was developed because that seems to be strongly at odds with the NSDUH survey data and trends in that data over the last several years, which to me again clearly says that menthol smokers, if anything, perceive their cigarettes to be more harmful, certainly not less harmful. And that's true of African-American smokers, as well as smokers generally.

So I'll just be interested to see how that conclusion, diametrically in disagreement with the NSDUH survey data, was developed.

DR. SAMET: Melanie, do you want to comment?

DR. WAKEFIELD: Sure. Just a quick comment, I think when asking questions about risk perception, you tend to get very different answers depending on the context you ask them in and exactly how you ask the question. And we paid a lot of attention to those sort of methodological issues for that very good reason.

I mean, in the last decade or so, there's been a huge amount of public education about the health risks of smoking, and so more than ever, consumers know that their cigarettes are harmful. So overall, we see an increase among all smokers, an acknowledgement that any smoking is harmful.

But asking a general question about whether smoking is harmful or whether cigarettes are harmful doesn't really speak to the research question of whether or not menthol cigarettes are more or less harmful than -- or perceived to be more or less harmful than non-menthol cigarettes. It's not a sensitive discriminator of consumers' beliefs.

In order to ask –- in order to get at that, you really need to ask the much more specific questions about the issues. So overall, I would think particularly in a climate where it's almost the politically correct response to say there's no difference or I'm not prepared to commit to a view about whether or not one type of cigarette is more harmful than another. The other thing that's been

going on in the last decade is quite a lot of coverage about light and mild cigarettes and the extent to which consumers may have been misled about the health risks of light and mild cigarettes.

So I think it's very, very important to look at how the questions are framed. And the way we've done that in the report I think helps us to really drill down into the information that is sensitive and helpful in coming to a conclusion about consumers' perceived risks and perceived harm of menthol cigarettes compared to non-menthol cigarettes.

DR. SAMET: Dan, to the same point?

DR. HECK: Yes. Just a small follow-up. I see there are other questions or comments as well. But with respect to that, the NSDUH survey, for instance, I can't really think of a more direct way to get at people's perceptions than to ask them that question. And that's exactly what was done across races and across the last two years.

DR. WAKEFIELD: Well, that's exactly the

problem, Dan, that it is a direct question. And in the conduit of a huge amount of public education in which people have been told that all cigarettes are harmful, it's not going to be a helpful question to talk to or speak to the comparative risks of menthol versus non-menthol cigarettes. It doesn't ask that question.

DR. SAMET: Jack?

DR. HENNINGFIELD: Dr. Wakefield and Dr. Heck, maybe you can help me here. But my understanding is that the industry approach was -- and I'm simplifying a little bit -- to ask the so-called direct question of populations, and as possible, where a population says something is more harmful than another population, whereas the basis for the conclusion was the perception within users, within the population that this ingredient contributed to a less harmful cigarette; in other words, one population could say my cigarettes are less harmful than another population but still believe that that ingredient makes their cigarette less harmful.

DR. SAMET: Melanie?

DR. WAKEFIELD: I think perhaps, just by way of clarification, this final section of the report I think really tries to emphasize that there's a big difference between what people say they think about reduced harm and how they actually feel or sense reduced harm.

People know that smoking is not good for their health, and if they're asked about whether they think menthol cigarettes are more or less harmful than non-menthol cigarettes, the vast majority of people are going to say there's no difference or they won't commit to a view, and we see that in the surveys. But the evidence also shows that consumers feel reassured by the sensory aspects of menthol cigarettes and by the menthol branding and marketing and labeling that contributes to these perceptions.

The product, the menthol product, is really the sum total of the marketing and the physical product itself; they go together. And the evidence shows that these sensed experiences of menthol

cigarettes are very closely related to lower perceived harm. It's reassuring to consumers. And I think that's what we need to come to grips with in the evidence.

DR. SAMET: Thank you. Patricia?

DR. HENDERSON: Melanie, I have a question. I know that among native Hawaiians and Pacific Islanders the rate of menthol smoking is quite high, especially among the youth. Was there any data out there that suggests that there was targeted marketing among this special population?

DR. WAKEFIELD: There wasn't a huge amount -- there weren't a huge amount of studies. There were very few studies on that particular population group. There was evidence that there has been I think some tailored messaging to Hawaiians and Pacific Islanders.

We found some of that in the tobacco industry documents, special messages around Hawaiian lifestyle and so forth associated with menthol marketing. But there just simply weren't enough studies for us to really form a conclusion

that this population has been much more targeted with menthol messages and marketing than non-menthol. So there was a daff of research, really, in that area.

DR. SAMET: Dan?

DR. HECK: Just a small follow-on there. Certainly the term “targeted marketing,” although it describes a very normal practice in competitive free enterprise, free markets, it does have a certain loaded sense here with a product that’s harmful and addicting as cigarette smoking is.

But I would remind the committee or request to the committee, in developing this draft to a final advisory opinion, to recall that the most relevant information on all of these topics is contemporary, current information, and information going forward. That will be the most important to FDA’s consideration.

I think the historical marketing practices have been much discussed and are worthy topics of academic study, but really bear little relevance to the FDA’s considerations going forward. And

certainly something like targeted marketing of youth or adolescence is against the law.

So I would just request of the committee -- I think our consideration would be most useful if we can consider the historical information, but to really focus on contemporary practices going forward.

DR. WAKEFIELD: If I might just respond, I think TPSAC was charged to look at all the evidence, and we did look at all the evidence related to menthol marketing and considered it as a whole. I think it's important to note that many people who are smokers today, and who would rather not be, smoke menthol cigarettes because of the tobacco marketing practices of past. So that's I think one thing that we need to bear in mind.

The other thing is that the branding and imagery used in tobacco marketing in years gone by is extremely powerful and it carries forward today in the continued use of cigarette brand names, and descriptive labels, and so forth. And having and maintaining a brand image that resonates with

consumers is critical for a cigarette brand, and it's critical for any product. This is just 101 marketing.

So I hear what you're saying, Dan, but I do think we have to think about it as a totality. And the past is not unconnected to the present.

DR. SAMET: Okay. Thanks. So we have three more.

Mark?

DR. CLANTON: Melanie, on the issue of looking at the data, we do run into problems, particularly with certain groups like on Pacific Islanders, where there are very small numbers in those available studies. But in the case of youth, I'm wondering, were you able to tease out anything based on youth surveys or youth data that describes their understanding of risk?

The reason I ask this question is, it is generally understood that youth, certainly between the ages of 10 and all the way up to 18, often have a different risk-perceived profile of almost any danger. And they tend to underestimate risk,

whether it's with respect to things that can cause physical injury, or drinking alcohol, or experimenting with drugs and/or tobacco. They tend to have a lower tendency to estimate less risk than really exists with those behaviors.

Was there anything in survey data or data you looked at that described the real risk perception of menthol cigarettes relative to non-menthol cigarettes in youth?

DR. WAKEFIELD: We found no empirical information on that subject. But I guess again, this is why I think the sensory kind of aspects of menthol are really important, because, in general, people rely on what they sense in their body to estimate or to perceive something that could be risky. And young people do that as much as anyone. And so I think when you have a product that tends to reduce -- something in the product that tends to reduce the irritation of cigarette smoke, making the smoke smoother and less harsh, it removes a barrier to doing something that is -- perhaps, going down a pathway of avoiding smoking in young

people. It facilitates a continuation of smoking, in fact.

So I think that's a particular aspect of menthol cigarettes that is most concerning. And I think the fact that marketing associated with menthol products promotes that sensory experience. It goes together as a package, that people expect to sense this or attend to it when they do use the product, somewhat more than they otherwise would perhaps.

DR. SAMET: Thank you. I don't know about anyone else. I'm having a little bit of trouble sometimes hearing Melanie.

DR. WAKEFIELD: I'm sorry.

DR. SAMET: I don't know whether you could be closer or further, or something, but experiment.

Let's see. Patricia?

DR. HENDERSON: Melanie, I have a quick question. But before I do that, I think history of any organization is important, Dr. Heck. And we would love to just kind of not think about American history about what has happened in the past, but we

are where we are because of what has happened in the past.

But, Melanie, I know that one of the industry provided documents on marketing shares per state. And based on that information, we know that the District of Columbia and I believe Hawaii were the top two states.

Did you look at any of that data?

DR. WAKEFIELD: I'm not bringing that to mind, Patricia, at the moment. Sorry.

DR. HECK: Just a small clarification, Patricia. I think there may have been menthol market shares but not marketing data by state, that I'm aware of.

DR. WAKEFIELD: That's probably why I'm not bringing it to mind. Thanks, Dan.

DR. SAMET: Jack?

DR. HENNINGFIELD: I guess more of a comment. I think the strength of the chapter and the analysis is the integration of historical data and current analyses in the same way to understand the problem of the decades of light and low tar

misrepresentation of those products. Those effects carry forward today and they are not over because the label is banned.

So I think that's a strength. And if we look at current data, we're faced with some facts that are consistent and some are the imagery, the green imagery and other healthy imagery that continues to be used to this day. And the second is the relative explosion of youth use and the proportion of use, which is not proof that that is because of health effects, but it is consistent with that. It's also consistent with contribution to addiction risk.

So I think to really understand the menthol problem, you have to look at both historical and contemporary data. And I think that is a strength here.

DR. SAMET: I think we've done this chapter.

Melanie, thank you. John?

DR. LAUTERBACH: Dr. Samet, there are a couple of references in this chapter to "work" and "press." When are these documents going to be made

available to us, so we can see what these references are? For example, at page 33, there's a reference to a report by Klausner, yet we have no citations to look that up and read it for ourselves.

DR. SAMET: Let's see. We did from Klausner, of course, when the team from UCSF presented. And my understanding is those papers are in press now in a supplement to tobacco control data. Copies have been provided I think, John, to you, apparently.

DR. WAKEFIELD: Yes. That's correct.

DR. SAMET: So I think that anything that is cited, other than the redacted material, is either in press and made available, but I don't think there are any documents, other than those redacted, for which materials have not been provided to this committee.

What we're going to do now is I think here is probably what will be a brief update on chapter 6 from Dorothy.

DR. HATSUKAMI: It's very brief. The

evidence synthesis that I presented at the last meeting is identical to what is in the chapter. So I certainly don't want to reiterate that. Currently, we're just doing some fine-tuning and editing. And hopefully, it'll be up on the website shortly. So that's it.

DR. SAMET: Could anybody possibly have questions on that presentation?

[No response.]

DR. SAMET: Last chance. Okay. Chapter 7, which is the chapter that Neal and I have authored, has been distributed in what was very close to a final form at our last meeting, and I think discussed now twice. And I think other than some minor editing and updating, I don't think there's much else to say about that chapter.

Neal, do you want to comment at all?

DR. BENOWITZ: There really is not very much of a change. I think what we did, we did change one of the conclusions about the relationship of menthol cigarettes on the metabolism of NNAL, just to say that there was insufficient evidence to say

that was more probable than not. But otherwise it was basically the same.

DR. SAMET: Any questions about chapter 7?

[No response.]

DR. SAMET: Okay. Good. And I suspect there might be questions about chapter 8, but it's not completed yet. And, again, of course that is, as I mentioned earlier, where we will provide the answers to the seven plus two questions, as well as overall findings and recommendations. So I'm going to provide this update of the chapters, and obviously everything is coming close to being done because March 23rd is six days away.

So let me ask if there are other general comments or questions about the draft chapters at this point.

[No response.]

DR. SAMET: Okay. Then we're actually I think on time for a break. And just let me remind the committee again not to discuss these matters during the break. And we'll reconvene at 3:00 p.m.

(Whereupon, a recess was taken.)

Open Public Hearing

DR. SAMET: Okay. We will now begin the open public hearing portion of the meeting. I'm going to read the following.

Both the Food and Drug Administration, FDA, and the public believe in a transparent process for information gathering and decision making. To ensure such transparency at the public open hearing session of the advisory committee meeting, FDA believes that it is important to understand the context of an individual's presentation. For this reason, FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement, to advise the committee of any financial relationship that you may have with the sponsor, its product, and, if known, its direct competitors.

For example, this financial information may include the sponsor's payment of your travel, lodging, or other expenses in connection with your attendance at the meeting. Likewise, the FDA encourages you at the beginning of your statement to advise the committee if you do not have any such

financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

The FDA and this committee place great importance in the open public hearing process. The insights and comments provided can help the agency and this committee in their consideration of the issues before them.

That said, in many instances and for many topics, there will be a variety of opinions. One of our goals today is for this open public hearing to be conducted in a fair and open way where every participant is listened to carefully and treated with dignity, courtesy, and respect. Therefore, please speak only when recognized by the chair. Thank you for your cooperation.

I believe that we have four commenters, beginning with Scott Ramminger --

MR. RAMMINGER: Yes. That's correct.

DR. SAMET: -- of the American Wholesale Marketers Association. And you'll get a warning at

two minutes, when there's two minutes left of your presentation time.

MR. RAMMINGER: Thank you, sir.

Hello. My name is Scott Ramminger. Thank you for the opportunity to speak today. I'm the president and CEO of the American Wholesale Marketers Association, and we're submitting this statement to express our serious concern that a ban on menthol cigarettes would be ineffective and create a significant contraband market with ill effects for our members and others, and one counter to the intended intent of FDA in this regard.

AWMA is the only international trade organization working on behalf of convenience distributors in the United States. Our members represent more than $85 billion in U.S. convenience products. Basically, our members wholesale all sorts of products -- candy and other products, including cigarettes -- to convenience stores.

Our membership also includes manufacturers, brokers, retailers, and others who are involved in the convenience product industry.

When Congress passed the tobacco control law, it handed FDA, and this advisory committee by extension, a set of important and demanding tasks affecting tobacco manufacturing, sales, and distribution.

AWMA has a front-row seat on many of the ramifications currently before TPSAC concerning whether to recommend banning menthol cigarettes. We are concerned about the very real possibility that banning menthol will only create a large contraband market.

AWMA's members are often affected by science-based policy decisions made by government regulatory bodies. While we are not experts on science, we do have grave concerns about whether the government agencies justify a regulatory action on a tenuous link or preconceived notion involving the product and its purported effect. On menthol, we take note that one of your draft reports said, and I quote, "The evidence is insufficient to conclude that smokers of menthol cigarettes face a different risk of tobacco-caused diseases than

smokers of non-menthol cigarettes." To our analysis, this appears to be a controlling conclusion. If menthol cigarettes have the same health effects as non-menthol cigarettes, how can the federal government justify a ban?

We believe it's right for TPSAC to look at proven science with solid data. Our members believe that the soundest and most comprehensive science should be an integral part of the public policy debate, impacting our industry and the nation as a whole. More importantly, to have the credibility with the public, government policies should always be built on the strongest science.

The question you face is this. What happens if a federal edict that lacks credibility with the public is issued? Common sense tells us that a decision that lacks credibility will be disregarded by the public and exploited by the black market operators. The result will adversely affect our members' livelihood, cost jobs, penalize the legitimate sellers of these products, encourage the creation of a black market, and probably make it

easier for young people to get their hands on cigarettes if they want to.

At AWMA, we have studied cigarette sales and contraband markets for years. As you know, menthol cigarettes today constitute about 30 percent of the national cigarette sales. If menthol were banned, the sales of a currently legal product would be replaced by a contraband product.

It's likely that this contraband market, because illicit trafficking of tobacco already exists in an established underground economy and will be sophisticated, large, and widespread. Our analysis tells us it's wrong to regard a black market as a single entity. And in fact, a new Government Accountability Office report on illicit tobacco issued this month proves that point by identifying the various illicit trade schemes that are currently used in today's black market.

The GAO said illicit trade schemes can originate at any point in the tobacco supply chain. It goes on to identify several ways illicit tobacco makes its way to consumers today from import and

export schemes to other avenues. The GAO does not address what would happen if menthol was banned, but the implication is clear to AWMA and its members. As the GAO noted, the contraband market is complex and constantly evolving. If menthol is banned, unregulated cigarettes would be inserted seamlessly into the black market.

An expanded black market would have many adverse effects. It would not only reduce the government's revenue, but also open the door for easy, unmonitored accessibility by youth. Organized criminal groups will be in the driver's seat, and black marketers will pocket billions in profit.

If contraband cigarettes are sold at lower prices, a distinct possibility given historical examples, it is likely that banning menthol will do little to diminish overall smoking. It's possible in fact to imagine a scenario where cheaper cigarettes that are avoiding taxes and a number of other regulatory costs paid by legitimate sellers could increase tobacco use among youths. And of

course, all these ramifications would directly affect jobs and the livelihood of our members and put those jobs in the hands of illegal sellers of product.

Thus, what will we gain if a decision regarding menthol is not based on sound science, lacks credibility, and ignores practical realities? Banning menthol will be good for illegal business and not much more. Plus, it stands a good chance of undermining the public health objectives.

In light of these realities, it's discouraging that this advisory committee did not, at its inception, endeavor to completely, comprehensively, and thoroughly study contraband markets. AWMA and others have brought forward, voluntarily, information of relevance. Still, any comprehensive attempt to meet a mandate of Congress would have benefitted from independent studies, testimony from government experts, and many more actions to fully inform your final advisory report.

AWMA believes strongly that it would be a mistake to deliberately create a contraband market

in the face of solid, scientific evidence that shows that menthol cigarettes have no different health effects than non-menthol cigarettes. Thank you very much for your time.

DR. SAMET: Okay. Thank you.

Questions? Mark?

DR. CLANTON: Mr. Ramminger -- is it Ramminger or Ramminger?

MR. RAMMINGER: Ramminger.

DR. CLANTON: Mr. Ramminger, TPSAC has heard a lot of testimony and also reviewed information on how precisely menthol levels are controlled and engineered by product. And we've also heard a lot of information on how those brands are positioned to compete against each other and differentiate each other one from another.

Do you believe that the exact same brands of menthol cigarettes that are available today would also be available to a black market?

MR. RAMMINGER: They might not be legitimate product, but we know that there's already a huge product of counterfeit cigarettes in this country.

Many of them are made in China and are basically indistinguishable from product that is made legitimately. You have to look at them with a microscope practically to tell the difference.

DR. CLANTON: So your major concern is about counterfeit cigarettes?

MR. RAMMINGER: Counterfeit and other sorts of black market product. I'm not certain that I could predict whether or not the counterfeiters would choose to counterfeit the most popular brand after it was banned. There'd be concern about counterfeit product, product obtained illegally in other markets or legally in other markets and brought into this market.

The point is that -– I mean, if you look at what -– you can look at -- not so much with menthol, but if you look at what has happened in Canada, which has regulated the cigarette industry very strongly -- I mean a huge percentage of the product reaching the market in Canada is black market product.

DR. CLANTON: Thank you.

DR. SAMET: Jack?

DR. HENNINGFIELD: Just a couple of points on the contraband market. First, I think that the Legacy Foundation report that we received had a pretty balanced and insightful analysis of the reality. And I think I'm not representing that report, but to highlight a couple of things that I think are important to keep in mind, the first is that when we hear about the contraband tobacco problem, that's not cigarettes mainly from China. That's American-made cigarettes smuggled from one state that's low tax to another state. The main way that we have a problem right now is with commercial cigarettes. It's not with cigarettes manufactured in backwoods factories.

Another point, the Canadian problem, which has come up a couple of times, a main way that that was fostered a decade or so ago was by cooperation in supply of cigarettes by a major tobacco company. In this country, to put the numbers in perspective, in the ballpark of a billion cigarettes are sold per day. Let's say 30 percent of them, let's say

300 million plus, are menthol. Depending on the size of the truck, that's someplace between 10 and 20 semi-truckloads of cigarettes. And that would mean, to come anything close to providing the menthol market with a contraband market, you're talking about getting truckloads of cigarettes every day, distributed to thousands of outlets that would be willing to sell a banned product.

So I think when we hear about some of these numbers, we have to keep in mind that there are some realities that -- I think, at least on my part, when I hear a lot of the discussion, I don't say anything because some of the numbers are so outrageous, and they're not consistent with the reality as I see it. I think the American Legacy Foundation report comes closer to reality.

One reality that we do have is around a third or 400,000 plus people dying who are smoking menthol cigarettes. And the question you have to ask is not necessarily just is that cigarette more deadly, but how many more people are smoking because of that type of cigarette? And how many

fewer would be smoking without that cigarette? And that's a point that is also missed in these discussions.

MR. RAMMINGER: Yes, sir. I guess in response to your comment, I would say, look, if you don't want to look at the examples I gave, consider prohibition. I mean, somehow, during prohibition, a lot of alcohol was manufactured and distributed in this country. Currently, in most states today, marijuana is illegal, and I can assure you that if any of you wanted to go out and try to find some, it wouldn't be that difficult.

The point is that whatever exists today, exists in a market where menthol is still legal. If you ban menthol with no scientific reason to do so, I believe strongly that a black market will develop to supply menthol cigarettes. I don't think there's any question about that.

DR. SAMET: Let me just comment about the you. It's not -- I think you said "If you ban menthol." Again, I would remind --

MR. RAMMINGER: I understand. I'm speaking

about the government.

DR. SAMET: Let me finish, please. Let me finish. My comment refers to the charge of TPSAC, and we are quite aware of our charge within the Act and what is required under Section 907(b) with regard to other considerations around contraband or other issues. And this will be considered in our report.

Again, I will just remind everyone that we have a very specific charge related to public health impact. Whatever actions may be taken by FDA, I think as Corinne outlined at the start of the session today, such matters lie in the hands of the FDA and not this committee. We recognize and don't need to be reminded of our role around the contraband issue.

I do have a question for you.

MR. RAMMINGER: Yes, sir?

DR. SAMET: You mentioned that your organization had done studies. Were those studies specific to menthol or to the contraband issue in general?

MR. RAMMINGER: They were the contraband issue in general, primarily on Internet acquisition of cigarettes illegally in this country.

DR. SAMET: I see. And let me ask, for those on the phone, Melanie and Neal, any questions?

DR. WAKEFIELD: I don't have any questions. Thanks, Jon.

DR. SAMET: Neal?

DR. BENOWITZ: I don't either, Jon. Thank you.

DR. SAMET: Any other questions from the committee or comments? Tim?

DR. MCAFEE: Just a follow-up on one of your analogies. Two things. One is you said that you can't see any point in banning menthol if there's no benefit to it because it would --

MR. RAMMINGER: In the absence of scientific evidence.

DR. MCAFEE: Yes. So my first question is, if there were science that showed, by our standards, which include the public health effect

that was alluded to -- in other words, that perhaps more people are initiating it and smoking because of menthol. Even if they're not more likely to get lung cancer, would you think that it would be a reasonable thing for society to do to ban it and then deal more aggressively? Because we certainly share most of your concerns about the existence of a contraband market.

The ultimate examples that you gave, like you gave the example of marijuana, and you basically said look, this is not being effective. But are you then proposing that you think that we would be better off as a society if we legalized marijuana, because we would then eliminate a contraband market?

MR. RAMMINGER: That's not within my purview.

DR. MCAFEE: Yes. I was actually going to suggest that you could certainly defer answering that question.

[Laughter.]

DR. MCAFEE: Could you answer the first

question?

MR. RAMMINGER: I did not inhale. The first question was --

DR. MCAFEE: The first question was, if there was --

MR. RAMMINGER: I mean, I would have -- that's a pretty hypothetical question. I don't understand exactly what -- if you're asking me if there were hard scientific evidence that menthol cigarettes were more harmful than non-menthol cigarettes?

DR. MCAFEE: Harmful in the public health sense, that more people -- like say according to this model, we'd save 60,000 lives a year if we banned menthol and tackled contraband.

MR. RAMMINGER: Well, I would have to look at the -- I would have to be convinced of the validity of the analysis. I don't think I can --

DR. MCAFEE: But if you determined it was valid, then you think it would be reasonable?

DR. SAMET: Tim, probably I think this is outside the scope of the comments he brought to us

Thank you. Thank you, Mr. Ramminger.

MR. RAMMINGER: Thank you, sir. Thank you all for listening.

DR. SAMET: Thank you.

Our next public commenter is William True from Lorillard Tobacco Company.

DR. TRUE: Good afternoon. Once again, my name is Bill True, and I'm the senior vice-president of research and development for Lorillard Tobacco Company, and I appreciate the opportunity to share a few thoughts with you this afternoon.

Today, I would like to focus on a very important topic related to the difference between smoking prevalence and smokers' preference for a certain type of cigarette. A number of recent headlines related to the posting of TPSAC's draft of chapter 4, Patterns of Menthol Cigarette Smoking, indicate that there is continued confusion over what prevalence and preference mean and whether they have population-level effects on public health.

One of the key questions raised by TPSAC is

whether the availability of menthol cigarettes increases the prevalence of smoking in the population. After analyzing the available data on this issue, the answer is clear to me, no. Yet, many reviews of the topic confuse cigarette preference and smoking prevalence, and have drawn inappropriate conclusions based on this misunderstanding.

Smoking prevalence provides estimates of cigarette use among the overall population; that is the proportion of individuals in a population or subpopulation that choose to smoke. For example, 21.3 percent of African Americans smoke, only 1 out of 5, which means that 4 out of 5 do not smoke. And to put that in context, the prevalence rate for white smokers is 22.1 percent, the same to slightly higher.

In contrast, cigarette-type preference provides information about the percentage of smokers who prefer a particular type of cigarette, such as full flavor, lower tar, menthol, or non-menthol.

As an example of the confusion of these terms that have been reported, yesterday the American Council on Science and Health printed a correction to its statement that, quote, “Over 80 percent of African Americans and more than half of Hispanics smoke menthol cigarettes.” In the correction, they acknowledge that over 80 percent of African Americans and more than half of Hispanic teenagers who smoke, smoke menthol cigarettes.

The distinction in terms is critical to understand because increases in smoking prevalence could have an impact on public health. However, increases in cigarette-type preference without increasing smoking prevalence would not have a public health impact.

Cigarette smoking in the overall population or prevalence has steadily declined during the last two decades, irrespective of race, ethnicity, gender, or age category. And these declines in smoking prevalence have generally been more pronounced for African Americans, despite their preference for menthol.

A few other points of emphasis. Non-menthol cigarettes are preferred by most smokers. Menthol cigarettes are preferred by some subgroups of smokers, particularly African Americans. Menthol smokers start smoking later in life. African-American menthol smokers start smoking substantially later than white menthol smokers. Menthol smokers typically smoke fewer cigarettes per day. Initiation rates are not increasing. The prevalence of African-American adolescent smoking is far below that of white adolescent smoking, about half, despite a dramatic preference for menthol cigarettes.

So in conclusion, evidence of higher menthol cigarette preference among specific demographic groups, including youth and younger adult smokers, does not translate to higher smoking prevalence or represent an increase in population-level harm.

Current cigarette-type preference is not informative with regard to the use of menthol versus non-menthol cigarettes during youth experimentation because 75 percent of all youth who

experiment with cigarette smoking choose not to become regular smokers. The NCI recently reported that cigarette smoking prevalence is declining for all demographic groups and that the declines have been more pronounced for minorities, females, and adolescents. Such declines in smoking prevalence, irrespective of changing in smoking preference, would be consistent with a reduction in population-level harm.

So to the question of whether the availability of menthol cigarettes increases the prevalence of smoking in the population, as a whole or among subgroups, the answer is absolutely not. Thank you.

DR. SAMET: Thank you. Questions? Can we check on the phone? Melanie or Neal?

DR. WAKEFIELD: Not from me.

DR. BENOWITZ: Not from me, either. Thank you.

DR. TRUE: Thank you.

DR. SAMET: Thank you very much.

Our next presenter is Jim Tozzi from the

Center for Regulatory Effectiveness.

MR. TOZZI: Good afternoon. Mr. Chairman, I applaud your statement that the role of the committee is risk assessment and not risk management.

I am Jim Tozzi. I'm with the Center for Regulatory Effectiveness. As you've heard a number of times, we're a regulatory watchdog that enforces or tries to enforce the good government statutes that regulate the regulators. And we're funded by virtually all sectors, industrial sectors, including the tobacco industry.

Now, as you've heard several times, my previous statements dealt with the adverse effects of contraband and some of them being on an order of magnitude greater than legal cigarettes. Today, I'm playing off a different chart and a different key. Today, I would like to move from the negative health effects of contraband tobacco to the fact and documented studies that contraband increases, dramatically, the access of youth to tobacco products.

I'm calling on the study of Professor Sara Hughes, who's at the Centre for Public Health, Faculty of Applied Health and Social Science at John Moores University in Liverpool, England. The title of her recent work was just published within the last year, is Smoking behaviours, access to cigarettes and relationships, 15- to 16-year-old schoolchildren. It was published in the European Journal of Public Health. And Dr. Hughes conducted this study for around 10,000 kids that were 15 to 16 years old.

Let me read her conclusions. First, "Among the heavier smokers, 49 percent purchased counterfeit cigarettes." She went on to reiterate the point that I've made several times. "Counterfeit products are more affordable than commercial cigarettes for young people on restricted incomes, and counterfeit cigarettes are known to contain higher levels of tar, nicotine, and carbon monoxide, as well as high toxic metal concentrations."

Now, the point that I'd like to emphasize is

her second conclusion. She says, “As with other European countries, a range of measures have been introduced or proposed in the U.K. to restrict access to cigarettes by adolescents and to control their promotion.”

Now, what was her conclusion? Her conclusion was strategies that restrict access to legal cigarettes among adolescents, increase their reliance on the use of counterfeit cigarettes.

Now, given that, I’ve heard a very extensive discussion you all had on chapter 4. And what is my interpretation of this study, in terms of the discussion you had on chapter 4 and youth access? It seems to me, if you want to reduce youth smoking, then you’re jumping on the wrong end of the teeter-totter. You should be jumping on controlling counterfeit flows and counterfeit cigarette sales, as opposed to all the apparent emphasis at the expense of that on restriction.

Now, why do I say that? I say it because sellers in the black market have no market segmentation. You never hear of a youth check when

the people sell loosies on the street on tobacco. No youth check. You just walk up and you buy them. So the huge studies suggest a circular relationship between access and youth consumption, meaning the greater access, the greater the youth consumption.

Now, I would like to address the second study that we examined, and it goes directly to the issue that Dr. Henningfield just raised in terms of contraband and the magnitude of it. And really, this was done by Dr. Turner of Glasgow Center for Child and Health Society in Scotland.

Now, she looked at two cohorts, too. And her conclusions were, “These findings suggest that variations in cigarette access may contribute to school differences in pupil smoking rates and that the relationship between access and adolescent smoking is circular, meaning with greater availability, there’s increasing rates and higher rates, enhancing access.”

So what does that mean with contraband? Smokers smoke more and a lot of people that didn’t smoke before now smoke. And I think it’s that

element of contraband that's not quantified that the committee should examine.

Now, where is all this contraband going to come from? And as you stated before, a lot of it is not China. But let me tell you, 400 billion cigarettes are produced a year in China. This is not my study. It's a study that just came out by a professor of Chinese origin called The Dragon that Breathes Smoke, Counterfeiting in the People's Republic of China. He documents 400 billion cigarettes per year, exported. Now, they go someplace, and I don't know where all the places they go, but a lot of them come here.

Now, what is 400 billion cigarettes in the amount of cigarettes you can think of? That supplies all of Great Britain for six years, to smoke. So those 400 billion cigarettes have been documented in a number of trade flows and it suggests that they're real and they're going someplace. He goes onto say that counterfeiting is the business of an organized criminal. And here's what's important. China has the largest population

of smokers in the world, some 300 million, “And it’s not surprising,” he says, and he documents this, “the biggest tobacco producer in the world is China, but it’s also one of the biggest exporters of tobacco.”

So what does the above statement lead me to believe, both of these studies, or three of them, and particularly the one that leads to this circular behavior between access and youth consumption? It seems to me that based on those studies, a menthol ban or serious product restrictions will in my mind have the following and cause the following issue.

It’s the fact that the Congress asked this committee and gave FDA the authority to regulate tobacco. And if you want to make a large dent in youth access based on the discussion that you had on chapter 4, and based on what I gave to me, it seems to me that you ought to go after the low-hanging fruit. And that is to ask your fellow agencies -- the Department of Justice and ATF -- to accord a higher priority to the enforcement of

contraband. It is not getting the priority that it should get in this country for a variety of reasons. And there's nothing that I know in the charter of this committee, as part of contraband, that it should not be given the same attention that you have on other things, mainly, the enforcement of contraband statutes.

Mr. Chairman, I yield the remainder of my time -- it's 22 seconds -- to you.

DR. SAMET: Thank you.

Questions? Mark?

MR. TOZZI: Yes, sir?

DR. CLANTON: Mr. Tozzi, it's always enjoyable hearing from you, so it's good to see you again today. I have a question about one of the things you were saying as a belief or based on your information. You were talking about how a black market would actually create greater access and even more smoking.

Was that roughly correct?

MR. TOZZI: Yes, sir. I quoted that one study. Right.

DR. CLANTON: I'm not going to try to test your memory because I happen to have the document here.

MR. TOZZI: I know. I made it available to everyone. I'm completely open.

DR. CLANTON: No, no.

MR. TOZZI: And that's why I provided it to the committee.

DR. CLANTON: I wanted to ask you to reflect on some testimony we heard from another group. These were two economists from the University of Chicago who presented a report from Lexicon, which I think was based on Newport data.

One of their conclusions was that in a black market, based on their assumptions, they came up with a number saying that A, there would be an increased cost of tobacco in a black market, and based on the price of elasticities they used, a 10 percent increase in cost would represent a 1 percent decrease in overall smoking rates.

It went on to create another scenario, saying a 50-percent increase in the cost of buying

tobacco on the black market could result in as high as a 3.5-percent overall decrease in smoking prevalence.

So I wanted to ask you, did you believe their assertions about actually decreases in smoking rates in a black market, or does your evidence point in a different direction?

MR. TOZZI: I did not do this study. I quoted it. I gave you the study that I quoted. And I think part of the issue or a difference in the two studies was what I think Dr. Heck asked the modeler this morning. It was those co-efficients of elasticity that they put in there, and I can't back those up one way or the other. I can say this, though, is that I have pretty good data on Ontario, and given their elasticities, when the price has increased, the black market increased. Fifty percent of the kids in Ontario now are counterfeit.

So I think that model that they used is a function of their price elasticities, and I can't verify them. But you're right, Dr. Clanton.

They're different than the two studies that I've just stated, undoubtedly.

DR. CLANTON: Thank you.

DR. SAMET: Other questions? On the phone, Melanie or Neal?

DR. WAKEFIELD: No. I'm fine. Thanks.

DR. BENOWITZ: No questions.

DR. SAMET: Thank you for your comments.

MR. TOZZI: Thank you for the question.

DR. SAMET: Next, our final speaker, Henry C. Alford [sic] from the National Black Chamber of Commerce.

MR. ALFORD: Thank you, sir. My name is Harry, please.

To the Tobacco Products Scientific Advisory Committee, good afternoon. I am Harry C. Alford, co-founder and president, CEO of the National Black Chamber of Commerce. I come before you today under my commitment to advocate for good policy that directly relates to the NBCC constituents and the African-American community as a whole.

In the work before you, the subcommittee has

a difficult task. With the enactment of the federal tobacco law, the government has a new tool to review and evaluate the health issues relating to cigarettes and other tobacco products. This is a powerful tool. I hope and pray that this is a tool you respect and that you plan to wield wisely.

In statements last year, the National Black Chamber of Commerce has already expressed its viewpoint that menthol is a rather inconsequential ingredient in a cigarette. NBCC has proudly warned the FDA about why banning menthol cigarettes would be wrong and would have unintended consequences. We also warned last year that a ban on menthol would create an underground contraband market in cigarettes and why this would be detrimental to the African-American community.

I'm speaking today about a specific concern that this advisory committee has not heeded the advice of the National Black Chamber of Commerce and many other groups to seriously assess the consequences of an underground market. We are frustrated, concerned and alarmed that the

committee forged ahead without developing an adequate record, that this committee has been seemingly cavalier about fulfilling a mandate of Congress to study contraband, and that it did not invite a host of experts to discuss this matter with you.

Let me be blunt. There are those who wonder whether the advisory committee declined to study the ramifications of an illicit market because it was afraid of the answers. I hope that this is not the case. Banning menthol, that is, creating a modern-day prohibition for the single product, would fuel an illicit market of unsafe, unregulated cigarettes.

Law enforcement agencies cannot keep pace today with the extensive underground market that already exists for contraband cigarettes. Studies show that many smokers would go to this illicit market for the cigarettes, or perhaps it is better to say that this illicit market would come to smokers. There would be buyers and sellers. The illicit market for tobacco would simply expand to

meet the need.

If menthol is banned, it is not a stretch to believe that the street sales would increase in black communities, the unregulated sales to minors would increase, and that large organized crime enterprises would corner the sales. When that happens, African Americans will be affected more than most.

First, a ban would adversely affect the African-American community because the government would mandate tougher arrests and enforcement efforts to control the market they created. The criminalization following that ban would fall most heavily on the black community. I surely hope this advisory committee does not want the FDA to set in motion a scenario in which our police, prosecutors, and judges end up spending their time dealing with an upsurge in contraband sales.

Second, small black-owned corner stores and businesses that rely on menthol sales to help make their payrolls each week will also suffer. Menthol sales are approximately 30 percent of the national

cigarette sales. In some urban communities, the figure is higher, which doesn't even count people who come into a convenience store to buy cigarettes but also get milk and bread.

Does the FDA want small business owners to suffer financially, all due to a decision based in scientific paternalism? It goes without saying that the intertwined issues of banning menthol cigarettes and illicit markets are ones of tremendous importance to African Americans.

The advisory committee's job is to present a credible recommendation to Americans in general, and specifically to black Americans. Your report should be justified on the sound science and comprehensive assessments, not flawed by preconceived notions or gaps in the public record.

It would be wrong to ban a product under a paternalistic justification that lacks scientific integrity or credibility. If that occurs, it will just come to be regarded as another ill-conceived government mandate aimed at a specific demographic profile.

Banning menthol in cigarettes should strike even the strongest anti-smokers, and certainly, many African Americans, is utterly beside the point. This is especially true when there's a lack of hard scientific evidence and when we celebrate an era in which Americans should have the right to personally choose among legal products.

No matter what you think of smoking, and I personally do not smoke cigarettes, the National Black Chamber of Commerce believes strongly that menthol is a rather inconsequential ingredient in a cigarette. Menthol simply is a taste preference preferred by African Americans and it should not be singled out for a ban. Thank you, sir. Thank you, Committee.

DR. SAMET: Thank you. I think perhaps just as a comment to both you and Mr. Tozzi, who I think began by commenting on the distinction between risk assessment and risk management, our task and our primary charge from Congress is to address the public health impact of menthol cigarettes, if any.

We are also charged with addressing a set of

other issues under Section 907(b), one of which includes the possibility of contraband. But I suggest that what we heard in your testimony and in the previous commenter, much of that perhaps will lie with further discussions or considerations, I think as Corinne Husten outlined in the initial slides about what this committee does and what FDA might do.

I think, again, your concerns are now a matter of the record and voiced. And I think FDA has heard from your organization and others who have voiced the same concerns. So I think the general concern about contraband has certainly been heard and it is not overlooked in our report.

Just to say again, as a reminder -- and I think you've been sitting here and seen it -- our approach to developing our report has been to turn to the scientific evidence in a very visible and open way. So I think what we're looking at is clear, and we've made clear what the scientific evidence is that we are evaluating. It's in fact laid out so that others can review the same

evidence. So we've tried to maintain transparency around our processes.

Let me see if there are questions or comments. Mark?

DR. CLANTON: Mr. Alford, thank you for taking time to testify.

MR. ALFORD: Yes, sir

DR. CLANTON: I know it takes some effort, and we're glad to hear from you. You mentioned, and it's been recognized elsewhere, that contraband, counterfeiting, black markets already exist with non-menthol tobacco products. I'm just curious, given your taking a stand on menthol, does your organization, the National Black Chamber of Commerce, have an existing official position on contraband, counterfeiting, black markets of non-menthol tobacco?

MR. ALFORD: Contraband is contraband, sir. We are against it.

DR. CLANTON: So you have an existing position that's been articulated before these meetings about contraband and black markets in non-

menthol cigarettes?

MR. ALFORD: We want our businesses to operate in a legal fashion and not be interfered with by outside sources that would make them non-competitive, such as bootlegging, knock-offs, whatever. Free trade in a regulated market should be existing. These outside sources have a detrimental impact on our businesses, and therefore, our jobs, employment figures.

DR. SAMET: Other questions? Patricia?

DR. HENDERSON: Mr. Alford, does your organization receive funding from any of the tobacco industry companies?

MR. ALFORD: Over the years, Altria was a member, not necessarily for their cigarettes. Lorillard has taken a membership. A membership into the National Black Chamber of Commerce is simply that, a membership. And we follow 501(c)(3) guidelines. We do not base policy on membership, and we have gone against members when we disagreed with their policy.

DR. SAMET: Other questions? On the phone,

Melanie or Neal?

DR. BENOWITZ: No.

DR. WAKEFIELD: None from me, thanks.

DR. HENDERSON: Mr. Alford, earlier, Dr. Mendez produced modeling for us targeting specifically for African Americans. Based on the numbers of saving between 44,000 and 66,000 lives within the next 50 -– the next 40 years in African-American communities, what does that number mean to you?

MR. ALFORD: I dispute that figure and that number because you stop a product, counterfeit will come in and replace that product. I daresay that if you stop menthol cigarettes, you will increase the deaths because you'd have contraband coming in, counterfeit coming in, not regulated, more dangerous, no telling what could be in it, and the price could be sky high. But they want it; they're going to get it. It's going to cost more, which means there's going to be less money for other means, and their health is probably going to be ruined because it's unsafe to begin with. You're

working against the whole concept.

DR. HENDERSON: Thank you.

DR. SAMET: Any other questions? Yes, Tim?

DR. MCAFEE: Again, thank you very much for speaking with us about this. And I'm just curious, because it seems like on the one hand you're saying that you think that menthol is a minor constituent of cigarettes and tobacco products, that it's a taste, a taste preference.

So I'm just curious. I'd say some of the polling data that has been presented here would suggest there's really nothing in it that would suggest that a large number of African-American smokers or menthol smokers in general would turn to a black market. And I think there's – and we don't really know because the only thing we have to go on is what's happened around price increases, which is dramatically different than a constituent. So people could quit. People could change brands to another, a non-menthol cigarette.

Again, I think we all would concur that this is a very important point that does need to be

addressed and that certainly the FDA will look into it. But I'm just curious what your evidence is that you think a large number of African Americans or other menthol users would actually turn to a black market as opposed to making some other choice.

MR. ALFORD: Sir, it's almost laughable. I've lived in Detroit. I've lived in Chicago. I grew up in metropolitan Los Angeles. And I see people take crack cocaine. I see people take heroin. I see people take anything illegal for a quick high and they die by the millions. And if you think we're going to all of a sudden get rigid and prudent in our choices, no.

DR. MCAFEE: So to be clear, you think that people are smoking menthol cigarettes in order to get menthol. They're not smoking it to get nicotine?

MR. ALFORD: They enjoy the taste of menthol, which is why they prefer cognac over Jim Beam. They enjoy the taste of cognac over Jim Beam. I'm talking about African Americans. They

buy Lexus, even if they can't afford a Lexus, because it's more enjoyable. If it weren't for the African-American community, Mercedes and Lexus would have a devastating drop in sales. That's just the way it is. I drive a Lexus, disclosure.

[Laughter.]

DR. SAMET: I was about to say, this is about cigarettes and not about cars.

[Laughter.]

MR. ALFORD: But if you cut it off, China will be happy. And they don't play by the rules. And if they see a profit, a market, they're going to take it. They're going to take advantage of it.

DR. SAMET: Okay. Thank you very much for your comments.

MR. ALFORD: Thank you.

DR. SAMET: Let's see. The open public hearing portion of this meeting is now concluded and we will no longer take comments from the audience. The committee will now turn its attention to address the task at hand, the careful consideration of the data before the committee, as

well as the public comments. And again, thank you to the public for your comments.

Dan, I now turn to you for the presentation of the menthol report from the industry perspective.

Menthol Report – Industry Perspective

DR. HECK: Thank you, Mr. Chairman. And I also want to thank the FDA staff for their efforts to get this draft executive summary of our forthcoming report before the committee today. This report will be issued and available within a few days. The report is complete. It's in the final stages of comment from various industry stakeholders. A report will be provided to FDA on time and I guess simultaneously provided to the committee and other interested persons.

The report was requested, the separate report from the industry, by FDA, as Dr. Husten has described. And I think this report should be quite useful to the FDA. It's a powerful report. It's an inclusive report. It's a soundly science-based analysis of all of the available data with emphasis

on the highest quality studies. It provides a full and I think balanced and defensible analysis of information that is available on this topic from academic research, from industry research, from government-funded research, as well as some of the government survey data that speak to some of the behavioral questions before the committee.

The report does focus on the question as specified in the statute, which is briefly recited here, to address whether menthol cigarettes have a disproportionate public health impact when compared to non-menthol cigarettes. That might be manifested either as increases of risk to the individual smoker, as well as to the general smoking population, or a subpopulation of smokers, or indeed to non-smokers in the fashion of any effect, any plausible effect on the increase of smoking initiation by former non-smokers.

The Congress also specifically recognized a need, as we heard a lot today in previous, for consideration of countervailing effects of a different regulatory approach to menthol, the

contraband, and the other issues. And that issue is also addressed in this report. I will briefly kind of walk through the process employed in this report to develop the final summary conclusions and then I'll just briefly itemize those conclusions. But since they're available to you in printed form, I won't read those explicitly in their complete form.

The report looks at the demographics of cigarette smoking. It looks at cigarette smoking, initiation, cessation, dependence, again, all these potential means in which menthol added to cigarettes might potentially impact the general public health.

The framework used to assess this diverse evidence is broadly based on that, employed by the surgeon general for some years now and developing inferences of causation for smoking-related diseases. These principles have been much discussed and I know are very familiar to the committee here. They're basically founded in the Bradford Hill criteria, which speaks to the

consistency and coherence and strength and specificity and the temporal relationship between a putative cause and a health outcome.

Certainly, the surgeon general's disease causation framework needs to be employed with some modification here because a big part of our consideration here asks us, in effect, to develop inferences of causation for the presence of menthol added to cigarettes as a cause of behaviors, behaviors like smoking initiation, increased smoking dependence, or cessation.

This is certainly a departure from the types of data normally considered in the surgeon general's and IOM and other types of considerations that have employed these principles, but I think the underlying principles are very robust and very well established for such considerations of diverse data.

The outcomes of the surgeon general's framework, briefly; I think we're all familiar with these. Evidence may be sufficient to infer a causal relationship; may be suggestive but

insufficient to make that conclusion; may be inadequate in the face of inconsistent, conflicting, or simply in the face of a shortage of relevant information. Importantly, the evidence may also be suggestive of no causal relationship.

The major conclusions of this report can be summarized. I will read this sentence. The report concludes -- using broadly the surgeon general's framework for assessing causality -- "The synthesis of the reliable data on the use of menthol in cigarettes leads to the conclusion that the evidence is suggestive of no causal relationship between menthol cigarettes and any disproportionate impact on the public health as a whole or for any demographic group when compared to non-menthol cigarettes." The individual conclusions supporting that overall conclusion will be itemized shortly.

The underlying facts in support of this conclusion are presented here briefly in the third page of the draft summary. We have looked at, largely from survey data, the information available to all of us on the initiation of smoking, smoking

dependence, and smoking cessation among populations. It has been said here many times, and we all are aware, that the majority of African-American smokers do prefer menthol cigarettes currently. And during the last two decades, though, the smoking prevalence generally has been in decline across racial groups, but that decline has been notably precipitous in African Americans.

The evidence from available epidemiology studies clearly demonstrates I think that menthol cigarettes are not inherently more risky, do not cause increases in disease risk to populations, and that's populations of smokers generally, as well as populations of both males and females and minority populations.

We have over a dozen epidemiology studies and some new ones becoming available right now, and we do not see an indication in a large, large majority of those studies of any increase and apparent risk.

So the conclusion there is that the evidence is suggestive of no causal relationship between the

addition of menthol to cigarettes and increased smoking-related disease risks.

There's a section on the biomarkers of smoke exposure, that we've received a lot of discussion here at the table. The evidence there on biomarkers of smoke exposure, as well as putative or potential biomarkers of risk, do not suggest increase risks or exposures attending to smoking menthol cigarettes.

So the conclusion of this discussion is that the evidence is suggestive of no causal relationship between the use of menthol in cigarettes and increases in biomarkers of exposure or potential harm over those caused by smoking non-menthol cigarettes.

The evidence on smoking topography -- that is, the intensity of smoking behavior and puffing, with regard to menthol is mixed. The evidence overall does not support a conclusion that menthol cigarettes are smoked more intensely. We don't have standard methods to examine this, so the literature, as we've discussed -- the findings of

those studies may be method dependent and there really isn't an ideal method available for us to measure how people may puff or smoke their cigarettes.

We do however have very measureable outcomes in terms of biomarkers, and I think that, in terms of quantitative measurements of smoking exposures attending smoking, I think we are best served by looking closely at the biomarkers evidence.

So the conclusion there with regard to smoking behavior is that evidence is inadequate to infer the presence or absence of a causal relationship with regard to our menthol cigarettes smoked differently, fundamentally, than non-menthol cigarettes.

We have a section on the toxicology and chemical properties of menthol cigarette smoke relative to non-menthol cigarettes. The available evidence here is quite straightforward and I don't think there can be much debate with the conclusion that we've offered that the evidence is suggestive of no causal relationship between menthol added to

cigarettes and increases in the toxicity of cigarette smoke, as we can measure it in experimental systems or the smoke chemistry of cigarette smoke; that is, menthol cigarettes have not been shown to have higher levels of toxic smoke constituents or some of the carcinogens, for instance.

The study also discusses in detail the studies that are available on smoking initiation with regard to menthol. And this includes, largely, survey studies that we've discussed at some length at this table.

Smoking initiation rates, as we've heard, have not changed significantly over the last decade, and some studies do indeed report that younger smokers have a high preference or a higher preference for menthol cigarettes than older smokers, but there really aren't any studies available that I'm aware of, or I think the committee's aware of, that directly examine the cigarette type, that is menthol versus non-menthol, that was employed at the time of smoking

initiation.

I guess out of necessity, the survey approaches have used surrogates of smoking initiation; that is, early smoking years, brand preference, because that's really the extent of the available information.

Our evaluation of this literature, reflecting also a lack of primary data in the area, is that the evidence is inadequate to infer the presence or the absence of a causal relationship between menthol cigarette use and adverse smoking initiation behaviors, including higher or earlier smoking initiation by the general population or by subpopulations.

As we've heard in some of the comments, menthol smokers tend to smoke fewer cigarettes per day and tend to start smoking or initiate smoking later in life, and those realities are reflected in the number of survey studies.

The industry report also examines the effect of menthol, or potential effect, on smoking cessation. The report reviews the methodologically

sound literature on smoking cessation. And the most relevant studies, those that address successful long-term smoking, are given a particular weight, and those do not indicate that smokers of menthol cigarettes are less likely to quit.

There are some studies, three cross-sectional studies and one draw from a smoking cessation clinic, that report lower smoking cessation rates among non-white menthol smokers only. We would expect that if menthol had a general effect on smoking cessation, that that would be manifested across races, sexes, and to smokers generally. And we do not see that pattern, so this I think suggests that the race associated in consistency indicates some other factor, possibly related to socioeconomic status or genetics, that affects the ability to quit.

I think we saw this in one of the clinical studies where employment status -- unemployed subjects had a significantly more difficult time quitting, and the employed subjects otherwise

similar were not significantly different in the reference groups. So I think we have factors at work here beyond the single factor of menthol in isolation. This leads to the conclusion that the evidence is suggestive of no causal relationship between the presence of menthol added to cigarettes and reduced cessation success.

A related topic -- in fact, they're entwined quite deeply -- with regard to nicotine dependence, or smoking dependence if you prefer, the analysis concludes that from the most methodologically sound literature, that menthol has no meaningful impact on nicotine dependence. This can be assessed or has been assessed by a variety of measures, including the intensity of cigarette consumption, cigarettes per day, time to first cigarette of the day, or the Fagerstrom test, or other related questionnaire-based assessments of the extent of dependence of smokers. As we mentioned previously, menthol smokers do not smoke more cigarettes per day and they do not really differ on composite measures of dependence such as the Fagerstrom test.

Given I think both the number of high quality studies and their overall consistent findings in this area, it's reasonable to conclude that the evidence is suggestive of no causal relationship between smoking menthol cigarettes and significantly increased nicotine dependence.

We've had a number of hypothesis discussed here at the table that in a way relate to some of the subject chapters here, but didn't quite fit in the analysis of the sound, scientific literature. So the report has presented several of these hypotheses for discussion in chapter 6. We don't think that the hypotheses nor the available information speaking to those hypotheses can serve as a basis for sound regulatory policy. And we regard those as speculative hypotheses that are perhaps worthy of some further investigation.

An example of that we've heard already today, the proposal that menthol smokers perceive their cigarettes to be less harmful than non-menthol smokers, again, I'll have to read the voting members' chapter here that I've just

received to understand the rationale that the voting members report uses to develop a conclusive opinion on this that the smokers do indeed perceive their cigarettes as less harmful, because, as I mentioned, the NSDUH survey has asked questions directly to smokers on this for some years and the trends have been very clear that indeed smokers do not perceive their cigarettes, menthol smokers, as less harmful; in fact, perceive them as more harmful in some of the analyses.

As I mentioned, we do have a discussion of the countervailing effects of a potential onerous regulatory action on menthol, and we've heard I think a lot about that today, and that topic is dealt with in the report.

So this report will, in full detail, be available to everyone within just a few days here. I think that any deep discussion of these will have to come from the actual text of the report, which is somewhat lengthy. It's not as long as it could be. It's not completely encyclopedic and inclusive because it's just too big a task. There's too much

literature, but the main reason why, as we've heard in a previous presentation, we had a quality analysis performed to try to help us prioritize the quality of the studies, particularly in the smoking behavioral area, the smoking initiation, dependence, and cessation area.

Since these types of studies aren't normally employed in the kind of surgeon general's type of deliberations, the criteria applied were those of the Agency for Healthcare Research and Quality, and it helped us to prioritize the studies, mainly the survey-type studies, for emphasis or de-emphasis in our analysis.

So I think that will give you at least a picture of what the industry report will entail, and I hope that the FDA will find it useful in their deliberations in the coming months and years. Thank you.

DR. SAMET: Thank you, Dan. I assume a few days means by March 23rd?

DR. HECK: Absolutely, before.

DR. SAMET: Before. Okay.

DR. HECK: On or about.

DR. SAMET: Actually, maybe just a couple points of clarification. In just reading about the report, it says it's submitted to FDA at its request by the non-voting industry representatives. So does that mean that it's coming from yourself, John, and Arnold?

DR. LAUTERBACH: Dr. Samet, we have not had a part in writing this. I have seen various sections, and I have seen nothing to disagree with.

MR. HAMM: I've reviewed sections of the report myself and will question the people -- or quiz the people I represent to see if they want to sign onto it.

DR. SAMET: It just may be -- having sort of asked this question before and recognizing that the answer might have been somewhat fluid, I wanted to make sure that we and the FDA understand -- and particularly in relationship to TPSAC members, whether you're sort of I guess authors, signers-on, or whatever or not.

DR. HECK: I'm a little unsure of that

myself. I would be pleased to discuss with the FDA. The understanding I have is that the report is probably best to be provided to the TPSAC mailbox electronically, but beyond that, I really don't know exactly how since it's unprecedented.

DR. SAMET: Right. But I think the point I was looking for clarification of really related to this sentence about saying it's submitted by the non-voting industry representatives and whether it is the three non-voting industry representatives, one, two, or three.

DR. HECK: I can try to answer that and the others can speak for themselves. I do apologize to my fellow representatives, as well as all of the numerous stakeholders because the final stage of making it available to the stakeholders for their review and comment has been more protracted than we originally envisioned.

But any industry stakeholders, companies, who wish to sign onto this are welcome to do so, and we'll be collecting that information. And we've heard from at least one of the companies,

Altria, who's indicated that they intend to file their own perspective. And I'm unaware of any others, but there could conceivably be other perspectives offered.

DR. SAMET: Thank you. I would just suggest that it be very clear in terms of the TPSAC representation, that this be sorted out.

One other question. Will this be a report -- in the second sentence, it says, "industry science with many decades of knowledge," and so on. So will this be a report with a listed committee of authors, or how will its origins be described?

DR. HECK: That wasn't our intent, but I guess I don't precisely know the answer to that yet. The report is presently a text like this with some appended tables, and the front matter and a cover letter or whatever has not been composed yet. But no. There wasn't a plan to identify individual contributors, who have been numerous.

DR. SAMET: Okay. I will just again say you might give consideration of that or to the extent

to which the report represents the work of consultants, just in terms of the transparency of the effort.

Just one other question. As you went through the sections of the report and the conclusions, I did not hear anything on menthol and the pharmacology of menthol. Is that covered in the report?

DR. HECK: Yes. That was in chapter 6 on some of the hypotheses that have been discussed at this table from the perspective of this industry report; the pharmacology, the mechanism of menthol, the cooling receptors. That's an interesting science, and I have an interesting flavor chemistry as well, so I find it quite interesting.

But we've heard the realities of this, the cigarettes, menthol cigarette manufacturing. These menthol cigarettes have been manufactured to meet the taste expectations of the consumers, and the levels of menthol in product are not set on any pharmacological basis. It's just a matter of taste preference.

So I think that the treatments we've seen, I think including in the voting members' report, of the pharmacology neurosensory topics relating to the mechanism of menthol's flavoring and cooling effects are interesting. But we have just basically, an itemization, an inventory of experimental observations from various experimental systems. But what we don't see is a clear connection of that mechanistic knowledge to cigarette smoking. So the industry report concludes that that speculative hypothesis that menthol cigarettes are uniquely cooling or soothing is not borne out.

DR. SAMET: Thanks. I think there must be other questions. Jack?

DR. HENNINGFIELD: Just a question on the scope of the literature. You mentioned the quality analysis that you had done. Is that the Covance analysis?

DR. HECK: Yes, it is. And that analysis has also been updated to include some of the later-appearing papers. So, yes. That was the quality

analysis used to help us consider the survey-type, behavioral-type studies, as opposed to the harder science, analytical chemistry, biomarkers, even epidemiology.

DR. HENNINGFIELD: So you followed that rigorously, but then -- I guess my concern is that analysis dismissed most of the literature I think a lot of which is highly relevant. It's just simply dismissive. And if you follow that rigorously, then you're ignoring a lot of the literature. Or was there literature that you selected that they dismissed or did you use anything that they dismissed?

DR. HECK: Your point is well taken, and I'm sure we've all had the same difficulty. Some of the studies that aren't of extremely high quality in terms of the ability to draw inferences for behaviors or -- relating to menthol in particular can't be ignored.

The quality filter or the quality analysis that was done gives us another facet to consider, but it wasn't a basis to, out of hand, ignore or

neglect a consideration of a study that has been impactful or has been received as discussion.

DR. HENNINGFIELD: The reason I'm asking is because some of that literature that was dismissed runs contrary to some of the conclusions that you appear to have. So it's going to be interesting to see how you supported it, which you ignored, and what literature you relied upon.

DR. HECK: Yes. And I think that brings up a very important point, that some of the conclusions in the literature, by this rigorous, independently performed quality analysis by published means, does not qualify as the kind of sound science that can really serve as a basis for regulatory decision making. So I think that the Covance report or the subsequent updated version will be very useful to FDA in their deliberations as well.

DR. HENNINGFIELD: Can I just point out that -- again, I haven't seen your report -- what literature are you relying on, which literature that you're considering not sufficient quality.

But in cases where there are differences, there can also be differences of opinion as to what is a quality study. And some of the studies that Covance rejected, I personally thought were high-quality studies by some of the best investigators in the world.

DR. HECK: The study quality criteria that were applied are described and are published, the Agency for Healthcare Research and Quality Standards. So that process was laid out, so the process is what it is. And, again, literature has not been of low quality by these standards and criteria, has not been excluded if it needs discussion. By the same token, studies that come out as high quality that really aren't that informative necessarily, we didn't overemphasize. But, again, all of these studies applied through this quality filter were those relating to these behaviors. These things are really harder to measure quantitatively in general.

DR. SAMET: Let me check on the phone. Melanie?

DR. WAKEFIELD: Yes. Dan, I don't see anything here on tobacco marketing. I mean, given the fact that tobacco marketing is so importantly related to youth, liking, initiation, in the general literature, I would have hoped that there would have been some attention given to that. I imagine that you have assigned that as to the hypothesis section. Would I be correct in assuming that?

DR. HECK: There is some discussion of marketing, and also just as for expediency sake, many prior written and presented presentations on the topic have been incorporated by reference, but there is some discussion of marketing. And, yes, it's in chapter 6, and I think there may be references elsewhere to that topic.

DR. WAKEFIELD: I'm not sure whether your comments earlier today would suggest that you have excluded or downplayed reference to earlier marketing practices by the tobacco industry.

DR. HECK: No. Not to any great extent. We think that FDA's deliberations, and indeed our

deliberations at the table here, as I stated earlier, are most usefully devoted to contemporary practices and certainly the practices going forward in the FDA-regulated environment, as opposed to studies from practices from decades ago.

DR. SAMET: Melanie, anything else?

DR. WAKEFIELD: That's all. Thank you.

DR. SAMET: Neal?

DR. BENOWITZ: I've got a couple questions. One is adolescents. You didn't talk about the adolescent studies, and obviously adolescence is a huge issue in terms of initiation and dependence. And some of the studies have been difficult to conduct, but there's still quite a body of literature.

Did you guys consider that?

DR. HECK: I apologize, Dr. Benowitz. Which studies? I didn't quite hear the question.

Did someone hear the question?

DR. SAMET: I think the question was -- go ahead, Neal. I'm sorry. Go ahead.

DR. BENOWITZ: I was just saying that an

important issue with respect to menthol is really the effect of menthol cigarette smoking among adolescence. And there are studies, they're relatively small studies, but there is quite a body of data, some of which looks pretty consistent even though they're small studies. I want to know whether you have addressed the adolescent literature in your review.

DR. HECK: Yes. Thank you. We have, indeed, and I'm sorry if I didn't reflect that accurately or completely in my brief comments here. But, yes. The subject of smoking initiation, and particularly, adolescent studies, is fully addressed in this report.

DR. BENOWITZ: Then a follow-up. When you talked about the pharmacology studies, I was wondering if you addressed the large body of tobacco industry documents, which really talk about menthol as cooling and helping people tolerate cigarettes, and the very interesting science that relates flavor and menthol to actually how people smoke cigarettes, so how many puffs they take,

their puff volume.

There's quite an interesting literature in the tobacco documents suggesting that really it's more than just a taste. It's really influencing, those relationships between menthol and flavor and how people smoke cigarettes.

DR. HECK: There is indeed some discussion of that. I'm generally aware that the literature, I haven't personally rigorously plowed through all of the internal industry research. It may not have been published.

I think the complicating factor in some of those documents is that there are a lot of speculations offered and interpretations of other outside literature offered by internal scientists for research purposes or whatever the purpose. But to the extent that that's not really distilled into conclusive published information or hasn't really been considered, I don't know that it has a place for undue consideration in a sound, science-based regulatory environment.

DR. SAMET: Neal, other questions?

DR. BENOWITZ: No. That's all.

DR. SAMET: Yes, Jack?

DR. HENNINGFIELD: Just a follow-up. There have been published studies based on tobacco industry research. And the area of document research, which is supported by NIH, is really a pretty sophisticated field now because it involves culling through the documents, trying to evaluate where there is enough literature that is consistent.

I guess my question is, are you dismissing all of the tobacco industry research as not meeting scientific standards, and so you didn't consider it?

DR. HECK: No. I think in fact I was referring primarily to some of the studies that you've mentioned, where persons have gone through the document archives and attempted to stitch together documents from various sources for various purposes sometimes. And I am personally familiar with a number of those, where the conclusions drawn by the academics in the field of document analysis

have been quite completely inaccurate and not correct.

So, no. I don't have, and the industry has not extensively referenced that literature because we found it to be an unreliable source of information for soundly scientific conclusions.

DR. HENNINGFIELD: The secondary analyses you considered unreliable, by the academic researchers, or the tobacco industry research you considered unreliable?

DR. LAUTERBACH: The secondary analyses, and the example we presented in July, the Kreslake 2008 paper, with the example of Newport, for example, the number one menthol. The manufacturer of Newport flatly, and without reservation, denied every conclusion in there drawn about Newport because they are simply incorrect. And not a single one of the referenced papers from the Newport manufacturer adequately and accurately supported the statement to which it was applied.

DR. SAMET: Tom, did you have a question?

DR. LAUTERBACH: Dr. Samet, I just want to

point out, in looking at the whole industry documents -- and I've been reviewing these from the time they first became available -- I know that there's statements that were attributed to people that had reported to me that were not supported by others, and certainly not by the experimental evidence we had. And, unfortunately, because the folks doing these academic reviews have not looked into the details and the qualifications of those making some of these statements, we just don't have a truly viable thing. And oftentimes, the scientists that knew the most are the ones you never find being quoted.

DR. SAMET: Dorothy?

DR. HATSUKAMI: Dan, in response to Neal Benowitz's question, you indicated that you were taking a look at -- or you had taken a look at the literature on the association between adolescence and menthol smoking and initiation. But I'm wondering whether you looked at dependence, because to me it seems like there is a consistent body of literature demonstrating that adolescents who do

smoke menthol cigarettes seem to be at higher risk for becoming more dependent or being more dependent than adolescents that smoke non-menthol cigarettes.

So I'm wondering if you did take a look at that literature.

DR. HECK: Yes, we did. And I think the difficulty here -- and I apologize for not having at my fingerprints all the answers to all these specifics because they are fully laid out in some detail in the written report. We heard a little earlier today about some of the confusion between a flavor preference or cigarette-type preference and the prevalence of smoking. And we've seen, to this day some confusion arising from that distinction.

This report does attempt to walk through that literature and to provide a useful and critical interpretation of the available literature. So in short answer, yes. That literature is addressed and we'll have that available within a few days.

DR. HATSUKAMI: This is addressing the urge or need to want a cigarette?

DR. HECK: Yes. And things such as the -- well, I mentioned the Fagerstrom test, but the standard instruments that are used to try to get at these behaviors that are so difficult to measure directly.

DR. SAMET: Dan, I have a general question -- and you know I'm quite familiar with the 2004 surgeon general's report -- the distinction between evidence suggestive of no causal relationship, and inadequate evidence.

So let me just ask you for example in the case of what is termed here the inherent health risks in the discussion of various diseases. And the conclusion of the evidence is suggestive of no causal relationship, but yet there are at most I think one or two studies on cardiovascular disease, the major killer associated with smoking and so on.

So how do you draw the line between no causal relationship, which would imply I think some certainty of knowledge that in fact there is no association versus an absence of evidence, which seems to me the case, certainly in the case of

cardiovascular disease, or COPD, and other major diseases. In fact, the major disease for which we have some body of information is lung cancer. And again, still a limited number of epidemiological studies.

So, to me at least, evidence suggestive of no causal relationship implies some certainty that there is no relationship, but, yet, for these key health outcomes, we just lack studies to this point.

So why did your group decide there was no causal relationship as opposed to inadequate evidence? I might raise the same concern for some of the other outcomes, but I think this one is particularly left out as I looked over this.

DR. HECK: Yes. I do agree with your concern that we only have two studies which get at cardiovascular and respiratory diseases, other than cancer, lung cancer. Some of the studies with general mortality may get at those, but I think that is an area that needs more attention.

I think it’s the consistency of the findings

among studies. Yes, we have something over a dozen, 12, 13, 14, something like that, including the ones that have not quite come to press yet. And of those, in terms of statistically significant findings, only one of the subanalyses in one of the studies -- that was the Sidney paper -- did report an elevated risk.

A number of those reported -- well, all of them reported, statistically insignificant differences in risk, and a few reported lower differences in risk, as we've discussed at this table previously, the Etzel 2008 paper most prominently, which I think is the most recent published epi study, case control study, of lung cancer in a model specific for African Americans. And the relative risk estimate, although not significant, was lower than 1.0.

I think it's just the consistency among studies and the coherence of the epidemiology literature with what we know from the smoking biomarkers and the other areas. I do think this is an area that's worthy of further work, but we do

have more epidemiology studies on menthol as a cigarette design variable than I believe any other one, with the possible exception of filtered/non-filtered cigarettes. You know that literature mostly emerged in the ‘70s, I guess. So although we never seem to have enough information, we do have quite a bit of information on menthol.

DR. SAMET: And, again, I guess maybe in part, consistency is in the eyes of the beholder. But it seems to be hard to evoke the notion of consistency, for example, for cardiovascular disease, given, at least on the epidemiology side, the very limited scope of evidence. I mean, with several studies, it’s hard to know what to expect.

DR. HECK: I do agree with you, sir. I think this is an area we need more work in. But just the consistency of the findings as being not statistically significant or balanced between finding lower apparent risk doesn’t suggest to me that there’s any basis to expect that menthol cigarettes may entail a greater cardiovascular risk. There’s no mechanistic basis for that I’m

familiar with. We have no compelling evidence of greater exposure. So it's difficult for me to identify a plausible mechanistic basis or biological plausibility of that. But, yes, I do think the area could use more work.

DR. SAMET: Other questions, comments?

DR. BENOWITZ: Jon, I've got one question.

DR. SAMET: Yes, Neal, please.

DR. BENOWITZ: Dan, the one concern that came out with the composition of the menthol cigarettes, when I look at the smoke, which was concerning to me and which was pretty consistent, was the 10-percent increase in particulates. And as I'm sure you know, there's a huge literature relating particulates to cardiovascular risk. There are no data on cardiovascular risk, but this was certainly a concern to me.

Did you look at that question?

DR. HECK: Were you referring to work by Battelle that's I don't think published, but was made available to us?

DR. BENOWITZ: No. I was talking about

several papers that were published I think by tobacco industry people, where they looked at composition of cigarettes with different casings added, including menthol casings, and showed that there was about a 10-percent increase in particulates. That was the same study that showed increased formaldehyde, but decreased other substances.

There was a discussion about why adding additives might increase particulates. So they speculated about mechanisms, but the observations seemed pretty clear, that particulates were increased by about 10 percent.

DR. HECK: I see what you mean. Yes, I understand your question now. By particulates, you mean the total particulate material, or TPM, the tar, if you will, tar plus moisture, in the smoke. Yes. The reason for that is that in these tests, experimental studies have been done with high levels of ingredients. An ingredient like menthol is transferred with very high efficiency into smoke. And it’s found -- it resides largely in the

particulate phase, despite its vapor pressure.

So what we see and have seen over the years in these high-level experimental studies, mainly, you're looking at the potential toxicology effects of added ingredients. We do see a greater particulate yield per cigarette, simply because the flavor ingredients like menthol transfer efficiently and near quantitatively into smoke in the intact form, as opposed to being pyrolyzed and turned into gaseous product.

So if I understand your question, there is a pretty clear understanding of the reason for that, and it's simply because the ingredients like menthol are transferred intact and contribute to the measured particulate phase.

DR. BENOWITZ: Right. But in follow-up to that, though, as I said, there is large literature about particulates in a non-specific way, not just tobacco particulates, but air pollution particulates and other particulates being a cardiovascular risk factor. So it seems to me, whatever the reason is, if you're generating more

particulates, then there is a potential increased risk.

DR. HECK: Yes. I understand what you're saying now. There is considerable literature on the carbon-based particulates such as atmospheric particulates. We have to remember, though, with the case of the cigarette smoke particulate phase, even though the term "particulates" is employed, these are really liquid droplets, so they don't have carbonaceous cores, as do the atmospheric particulates, and they impact in the respiratory tract and dissolve and are absorbed in a different manner. They don't remain more or less intact and are taken up as particulates by phagocytosis in the epithelium.

DR. SAMET: Other comments? John, did you have a comment? No?

[No response.]

DR. SAMET: Let me see. Are there any other comments about the initial look at the industry report?

[No response.]

Adjournment

DR. SAMET: Thank you, then. Actually, we've reached the end of our agenda for the day.

Just as a reminder, we start at 8:00 a.m. tomorrow, and there we will be going through the remaining chapter, chapter 8, probably returning to some discussion of chapter 6, and offering our recommendations, describing our recommendations, to FDA. So I will see you all in the morning at 8:00 here, sharp. Thank you.

(Whereupon, at 4:50 p.m., the meeting was adjourned.)